09/297895

510 Rec'd PCT/PTO 07 MAY 1999

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PCT application of PURDUE RESEARCH FOUNDATION	) Authorized Officer: Paul F. Urrutia
International Application Number PCT/US97/20539	) Mailing Date 28 January 1998
International Filing Date 07 November 1997	) Agent's File Reference: PUR-63/75P
Title of Invention PARTICLE ANALYSIS SYSTEM AND METHOD	)

RESPONSE TO INVITATION TO CORRECT DEFECTS

Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Attn: RO/US

Dear Sir/Madam:

In response to the Invitation to Correct Defects in the International application mailed 29 December 1997, Applicant submits herewith eight duly executed Appointments of Agent, new substitute description, claims and abstract and Sheet 3 of the Request correcting the spelling of Jeffrey Kao's first name. In the course of correcting the Description, a printing error was noted regarding equations (10) and (18). Specifically, stray characters were printed instead of the intended ellipses. These errors

"Express Mail" label number EM566458501US
Date of Deposit 28 January 1998
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37CFR § 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Signature of person mailing paper or fee

have also been corrected. The ellipses were properly included in the same equations of the U.S. Patent application Serial No. 08/747,112 from which priority is claimed and which was incorporated by reference in the PCT application as originally filed on page 56 and as amended on page 64. Thus it is believed that this subject matter is not being newly added. We believe that this application conforms to the requirements of the PCT.

Respectfully submitted

By L. Scott Paynter

L. Scott Paynter, #39,797
Woodard, Emhardt, Naughton,
Moriarty & McNett
Bank One Center/Tower, Suite 3700
111 Monument Circle
Indianapolis, Indiana 46204 US
(317) 634-3456

Enclosures: Eight Appts. Of Agent, substitute pages of Description, Claims and Abstract and Sheet 3 of Request

wenmm\sys\groups\frgnfile\pct\pur63.75inv

PATENT COOPERATION TREATY

Appointment of Agent or Common Representative

The undersigned applicant, PURDUE RESEARCH FOUNDATION, hereby appoints Harold R. Woodard, No. 16,214; C. David Emhardt, No. 18,483; Joseph A. Naughton, Jr., No. 19,814; John V. Moriarty, No. 26,207; John C. McNett, No. 25,533; Thomas Q. Henry, No. 28,309; James M. Durlacher, No. 28,840; Charles R. Reeves, No. 28,750; Vincent O. Wagner, No. 29,596; Steve Zlatos, No. 30,123; Spiro Bereveskos, No. 30,821; William F. Bahret, No. 31,087; Clifford W. Browning, No. 32,201; R. Randall Frisk, No. 32,221; Daniel J. Lueders, No. 32,581; Michael D. Beck, No. 32,722, Kenneth A. Gandy, No. 33,386; Timothy N. Thomas, No. 35,714; Kerry P. Sisselman, No. 37,237; Kurt N. Jones, No. 37,996; John H. Allie, No. 39,088; Jeffrey A. Michael, No. 37,394; Holiday W. Banta, No. 40,311; Troy J. Cole, No. 35,102; L. Scott Paynter, No. 39,797; J. Andrew Lowes, No. 40,706; Darrin Wesley Harris, No. 40,636; Matthew R. Schantz, No. 40,800; Gregory B. Coy, 40,967; Lisa A. Hiday, No. 40,036; John V. Daniluck, 40,581 and James L. Rowe, No. 18,448, all of the same address and who are members of the Bar of the State of Indiana, constituting the firm of Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, Indiana 46204 United States of America

[X] as agent [ ] as common representative

to act on its behalf before the competent International Authorities in connection with the international application concerning PARTICLE ANALYSIS SYSTEM AND METHOD, Agent's File Reference PUR-63/75P, International Application Number unknown at this time, filed with the United States receiving office and to receive payments on its behalf.

(Place) West Lafayette, IN (Date) DEC 15 1997

PURDUE RESEARCH FOUNDATION

Bruce L. Pershing

Bruce PERSHING
Secretary

PATENT COOPERATION TREATY
Appointment of Agent or Common Representative

The undersigned applicant, Eva SEVICK-MURACA, hereby appoints Harold R. Woodard, No. 16,214; C. David Emhardt, No. 18,483; Joseph A. Naughton, Jr., No. 19,814; John V. Moriarty, No. 26,207; John C. McNett, No. 25,533; Thomas Q. Henry, No. 28,309; James M. Durlacher, No. 28,840; Charles R. Reeves, No. 28,750; Vincent O. Wagner, No. 29,596; Steve Zlatos, No. 30,123; Spiro Bereveskos, No. 30,821; William F. Bahret, No. 31,087; Clifford W. Browning, No. 32,201; R. Randall Frisk, No. 32,221; Daniel J. Lueders, No. 32,581; Michael D. Beck, No. 32,722, Kenneth A. Gandy, No. 33,386; Timothy N. Thomas, No. 35,714; Kerry P. Sisselman, No. 37,237; Kurt N. Jones, No. 37,996; John H. Allie, No. 39,088; Jeffrey A. Michael, No. 37,394; Holiday W. Banta, No. 40,311; Troy J. Cole, No. 35,102; L. Scott Paynter, No. 39,797; J. Andrew Lowes, No. 40,706; Darrin Wesley Harris, No. 40,636; Matthew R. Schantz, No. 40,800; Gregory B. Coy, 40,967; Lisa A. Hiday, No. 40,036; John V. Daniluck, 40,581 and James L. Rowe, No. 18,448, all of the same address and who are members of the Bar of the State of Indiana, constituting the firm of Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, Indiana 46204 United States of America

[X] as agent [ ] as common representative

to act on his/her behalf before the competent International Authorities in connection with the international application concerning PARTICLE ANALYSIS SYSTEM AND METHOD, Agent's File Reference PUR-63/75P, International application Number unknown at this time, filed with the United States receiving office and to receive payments on his/her behalf.

(Place) West Lafayette, Indiana (Date) November 30, 1997

Eva Sevick-Muraca

Name: Eva SEVICK-MURACA

PATENT COOPERATION TREATY
Appointment of Agent or Common Representative

The undersigned applicant, Joseph PIERCE, hereby appoints Harold R. Woodard, No. 16,214; C. David Emhardt, No. 18,483; Joseph A. Naughton, Jr., No. 19,814; John V. Moriarty, No. 26,207; John C. McNett, No. 25,533; Thomas Q. Henry, No. 28,309; James M. Durlacher, No. 28,840; Charles R. Reeves, No. 28,750; Vincent O. Wagner, No. 29,596; Steve Zlatos, No. 30,123; Spiro Bereveskos, No. 30,821; William F. Bahret, No. 31,087; Clifford W. Browning, No. 32,201; R. Randall Frisk, No. 32,221; Daniel J. Lueders, No. 32,581; Michael D. Beck, No. 32,722, Kenneth A. Gandy, No. 33,386; Timothy N. Thomas, No. 35,714; Kerry P. Sisselman, No. 37,237; Kurt N. Jones, No. 37,996; John H. Allie, No. 39,088; Jeffrey A. Michael, No. 37,394; Holiday W. Banta, No. 40,311; Troy J. Cole, No. 35,102; L. Scott Paynter, No. 39,797; J. Andrew Lowes, No. 40,706; Darrin Wesley Harris, No. 40,636; Matthew R. Schantz, No. 40,800; Gregory B. Coy, 40,967; Lisa A. Hiday, No. 40,036; John V. Daniluck, 40,581 and James L. Rowe, No. 18,448, all of the same address and who are members of the Bar of the State of Indiana, constituting the firm of Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, Indiana 46204 United States of America

[X] as agent [ ] as common representative

to act on his/her behalf before the competent International Authorities in connection with the international application concerning PARTICLE ANALYSIS SYSTEM AND METHOD, Agent's File Reference PUR-63/75P, International application Number unknown at this time, filed with the United States receiving office and to receive payments on his/her behalf.

(Place) Kimberly WI (Date) 12/16/97

Joseph Pierce

Name: Joseph PIERCE

PATENT COOPERATION TREATY
Appointment of Agent or Common Representative

The undersigned applicant, Steven RICHTER, hereby appoints Harold R. Woodard, No. 16,214; C. David Emhardt, No. 18,483; Joseph A. Naughton, Jr., No. 19,814; John V. Moriarty, No. 26,207; John C. McNett, No. 25,533; Thomas Q. Henry, No. 28,309; James M. Durlacher, No. 28,840; Charles R. Reeves, No. 28,750; Vincent O. Wagner, No. 29,596; Steve Zlatos, No. 30,123; Spiro Bereveskos, No. 30,821; William F. Bahret, No. 31,087; Clifford W. Browning, No. 32,201; R. Randall Frisk, No. 32,221; Daniel J. Lueders, No. 32,581; Michael D. Beck, No. 32,722, Kenneth A. Gandy, No. 33,386; Timothy N. Thomas, No. 35,714; Kerry P. Sisselman, No. 37,237; Kurt N. Jones, No. 37,996; John H. Allie, No. 39,088; Jeffrey A. Michael, No. 37,394; Holiday W. Banta, No. 40,311; Troy J. Cole, No. 35,102; L. Scott Paynter, No. 39,797; J. Andrew Lowes, No. 40,706; Darrin Wesley Harris, No. 40,636; Matthew R. Schantz, No. 40,800; Gregory B. Coy, 40,967; Lisa A. Hiday, No. 40,036; John V. Daniluck, 40,581 and James L. Rowe, No. 18,448, all of the same address and who are members of the Bar of the State of Indiana, constituting the firm of Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, Indiana 46204 United States of America

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to act on his/her behalf before the competent International Authorities in connection with the international application concerning PARTICLE ANALYSIS SYSTEM AND METHOD, Agent's File Reference PUR-63/75P, International application Number unknown at this time, filed with the United States receiving office and to receive payments on his/her behalf.

(Place) West Lafayette, Indiana (Date) December 2, 1997

Steven Richter

Name: Steven RICHTER

PATENT COOPERATION TREATY
Appointment of Agent or Common Representative

The undersigned applicant, Rajesh SHINDE, hereby appoints Harold R. Woodard, No. 16,214; C. David Emhardt, No. 18,483; Joseph A. Naughton, Jr., No. 19,814; John V. Moriarty, No. 26,207; John C. McNett, No. 25,533; Thomas Q. Henry, No. 28,309; James M. Durlacher, No. 28,840; Charles R. Reeves, No. 28,750; Vincent O. Wagner, No. 29,596; Steve Zlatos, No. 30,123; Spiro Bereveskos, No. 30,821; William F. Bahret, No. 31,087; Clifford W. Browning, No. 32,201; R. Randall Frisk, No. 32,221; Daniel J. Lueders, No. 32,581; Michael D. Beck, No. 32,722, Kenneth A. Gandy, No. 33,386; Timothy N. Thomas, No. 35,714; Kerry P. Sisselman, No. 37,237; Kurt N. Jones, No. 37,996; John H. Allie, No. 39,088; Jeffrey A. Michael, No. 37,394; Holiday W. Banta, No. 40,311; Troy J. Cole, No. 35,102; L. Scott Paynter, No. 39,797; J. Andrew Lowes, No. 40,706; Darrin Wesley Harris, No. 40,636; Matthew R. Schantz, No. 40,800; Gregory B. Coy, 40,967; Lisa A. Hiday, No. 40,036; John V. Daniluck, 40,581 and James L. Rowe, No. 18,448, all of the same address and who are members of the Bar of the State of Indiana, constituting the firm of Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, Indiana 46204 United States of America

[X] as agent [ ] as common representative

to act on his/her behalf before the competent International Authorities in connection with the international application concerning PARTICLE ANALYSIS SYSTEM AND METHOD, Agent's File Reference PUR-63/75P, International application Number unknown at this time, filed with the United States receiving office and to receive payments on his/her behalf.

(Place) West Lafayette, IN (Date) January 07, 1998

Rajesh Shinde

Name: Rajesh SHINDE

PATENT COOPERATION TREATY
Appointment of Agent or Common Representative

The undersigned applicant, Ganesh BALGI, hereby appoints Harold R. Woodard, No. 16,214; C. David Emhardt, No. 18,483; Joseph A. Naughton, Jr., No. 19,814; John V. Moriarty, No. 26,207; John C. McNett, No. 25,533; Thomas Q. Henry, No. 28,309; James M. Durlacher, No. 28,840; Charles R. Reeves, No. 28,750; Vincent O. Wagner, No. 29,596; Steve Zlatos, No. 30,123; Spiro Bereveskos, No. 30,821; William F. Bahret, No. 31,087; Clifford W. Browning, No. 32,201; R. Randall Frisk, No. 32,221; Daniel J. Lueders, No. 32,581; Michael D. Beck, No. 32,722, Kenneth A. Gandy, No. 33,386; Timothy N. Thomas, No. 35,714; Kerry P. Sisselman, No. 37,237; Kurt N. Jones, No. 37,996; John H. Allie, No. 39,088; Jeffrey A. Michael, No. 37,394; Holiday W. Banta, No. 40,311; Troy J. Cole, No. 35,102; L. Scott Paynter, No. 39,797; J. Andrew Lowes, No. 40,706; Darrin Wesley Harris, No. 40,636; Matthew R. Schantz, No. 40,800; Gregory B. Coy, 40,967; Lisa A. Hiday, No. 40,036; John V. Daniluck, 40,581 and James L. Rowe, No. 18,448, all of the same address and who are members of the Bar of the State of Indiana, constituting the firm of Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, Indiana 46204 United States of America

[X] as agent [ ] as common representative

to act on his/her behalf before the competent International Authorities in connection with the international application concerning PARTICLE ANALYSIS SYSTEM AND METHOD, Agent's File Reference PUR-63/75P, International application Number unknown at this time, filed with the United States receiving office and to receive payments on his/her behalf.

(Place) West Lafayette, Indiana (Date) December 2nd 1997

Name: Ganesh BALGI

PATENT COOPERATION TREATY
Appointment of Agent or Common Representative

The undersigned applicant, Jeff~~ery~~ re KAO, hereby appoints Harold R. Woodard, No. 16,214; C. David Emhardt, No. 18,483; Joseph A. Naughton, Jr., No. 19,814; John V. Moriarty, No. 26,207; John C. McNett, No. 25,533; Thomas Q. Henry, No. 28,309; James M. Durlacher, No. 28,840; Charles R. Reeves, No. 28,750; Vincent O. Wagner, No. 29,596; Steve Zlatos, No. 30,123; Spiro Bereveskos, No. 30,821; William F. Bahret, No. 31,087; Clifford W. Browning, No. 32,201; R. Randall Frisk, No. 32,221; Daniel J. Lueders, No. 32,581; Michael D. Beck, No. 32,722, Kenneth A. Gandy, No. 33,386; Timothy N. Thomas, No. 35,714; Kerry P. Sisselman, No. 37,237; Kurt N. Jones, No. 37,996; John H. Allie, No. 39,088; Jeffrey A. Michael, No. 37,394; Holiday W. Banta, No. 40,311; Troy J. Cole, No. 35,102; L. Scott Paynter, No. 39,797; J. Andrew Lowes, No. 40,706; Darrin Wesley Harris, No. 40,636; Matthew R. Schantz, No. 40,800; Gregory B. Coy, 40,967; Lisa A. Hiday, No. 40,036; John V. Daniluck, 40,581 and James L. Rowe, No. 18,448, all of the same address and who are members of the Bar of the State of Indiana, constituting the firm of Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, Indiana 46204 United States of America

[X] as agent [ ] as common representative

to act on his/her behalf before the competent International Authorities in connection with the international application concerning PARTICLE ANALYSIS SYSTEM AND METHOD, Agent's File Reference PUR-63/75P, International application Number unknown at this time, filed with the United States receiving office and to receive payments on his/her behalf.

(Place) Houston, TX (Date) 12-29-97

Jeffrey Kao

Name: Jeff~~ery~~ re KAO

PATENT COOPERATION TREATY
Appointment of Agent or Common Representative

The undersigned applicant, Huabei JIANG, hereby appoints Harold R. Woodard, No. 16,214; C. David Emhardt, No. 18,483; Joseph A. Naughton, Jr., No. 19,814; John V. Moriarty, No. 26,207; John C. McNett, No. 25,533; Thomas Q. Henry, No. 28,309; James M. Durlacher, No. 28,840; Charles R. Reeves, No. 28,750; Vincent O. Wagner, No. 29,596; Steve Zlatos, No. 30,123; Spiro Bereveskos, No. 30,821; William F. Bahret, No. 31,087; Clifford W. Browning, No. 32,201; R. Randall Frisk, No. 32,221; Daniel J. Lueders, No. 32,581; Michael D. Beck, No. 32,722, Kenneth A. Gandy, No. 33,386; Timothy N. Thomas, No. 35,714; Kerry P. Sisselman, No. 37,237; Kurt N. Jones, No. 37,996; John H. Allie, No. 39,088; Jeffrey A. Michael, No. 37,394; Holiday W. Banta, No. 40,311; Troy J. Cole, No. 35,102; L. Scott Paynter, No. 39,797; J. Andrew Lowes, No. 40,706; Darrin Wesley Harris, No. 40,636; Matthew R. Schantz, No. 40,800; Gregory B. Coy, 40,967; Lisa A. Hiday, No. 40,036; John V. Daniluck, 40,581 and James L. Rowe, No. 18,448, all of the same address and who are members of the Bar of the State of Indiana, constituting the firm of Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, Indiana 46204 United States of America

[X] as agent [ ] as common representative

to act on his/her behalf before the competent International Authorities in connection with the international application concerning PARTICLE ANALYSIS SYSTEM AND METHOD, Agent's File Reference PUR-63/75P, International application Number unknown at this time, filed with the United States receiving office and to receive payments on his/her behalf.

(Place) Clemson, SC (Date) December 12, 1997

Name: Huabei JIANG

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International Bureau

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(71) Applicant *(for all designated States except US)*: PURDUE RESEARCH FOUNDATION [US/US]; Office of Technology Transfer, 1650 Engineering Administration Building, Room 328 ENAD, West Lafayette, IN 47906 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: SEVICK-MURACA, Eva [US/US]; 7650 E. 100 N., Lafayette, IN 47905 (US). PIERCE, Joseph [US/US]; 309 Juniper Street, Lake Jackson, TX 77566 (US). RICHTER, Steven [US/US]; 16 Queens Court, Brunswick, GA 31521 (US). SHINDE, Rajesh [IN/US]; 1901 Union Street #126, Lafayette, IN 47904 (US). BALGI, Ganesh [IN/US]; 246 Longley Drive, Lebanon, IN 46052 (US). KAO, Jeffrey [US/US]; 301 Huckleberry Drive, Lake Jackson, TX 77566 (US). JIANG, Huabei [CN/US]; 205–05 Airport Road, West Lafayette, IN 47906 (US).

(74) Agents: PAYNTER, L., Scott et al.; Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, IN 46204 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

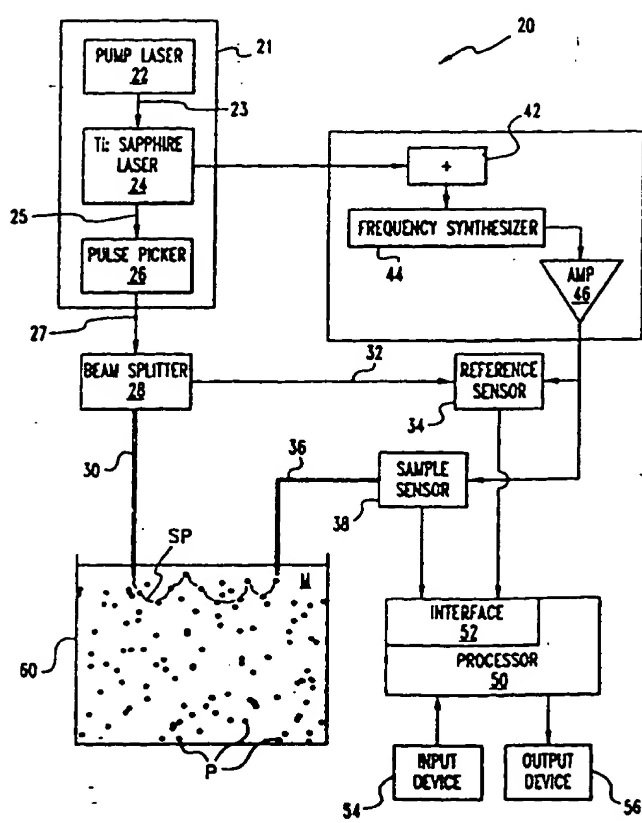
With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: PARTICLE ANALYSIS SYSTEM AND METHOD

(57) Abstract

A system (20) and method are disclosed for the self–calibrating, on–line determination of size distribution f(x) and volume fraction ϕ of a number of particles (P) dispersed in a medium (M) by detecting one or more propagation characteristics of multiply scattered light from the particles (P). The multiply scattered light is re–emitted in response to exposure to a light source (21) configured to provide light at selected wavelengths. The determination includes calculating the isotropic scattering and absorption coefficients for the particles (P) by comparing the incident and detected light to determine a measurement corresponding to the propagation time through the scattering medium (M), and iteratively estimating the size distribution f(x) and volume fraction ϕ as a function of the coefficients for each of the wavelengths. An estimation approach based on an expected form of the distribution and the mass of the particles is also disclosed. Furthermore, techniques to determine a particle structure factor indicative of particle–to–particle interactions which vary with particle concentration and influence light scattering at high concentrations is disclosed.



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HU	Hungary
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KP	Democratic People's Republic of Korea
KR	Republic of Korea
KZ	Kazakstan
LC	Saint Lucia
LI	Liechtenstein
LK	Sri Lanka
LR	Liberia
LS	Lesotho
LT	Lithuania
LU	Luxembourg
LV	Latvia
MC	Monaco
MD	Republic of Moldova
MG	Madagascar
MK	The former Yugoslav Republic of Macedonia
ML	Mali
MN	Mongolia
MR	Mauritania
MW	Malawi
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SE	Sweden
SG	Singapore
SI	Slovenia
SK	Slovakia
SN	Senegal
SZ	Swaziland
TD	Chad
TG	Togo
TJ	Tajikistan
TM	Turkmenistan
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TT	Trinidad and Tobago
UA	Ukraine
UG	Uganda
US	United States of America
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VN	Viet Nam
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94 12/106

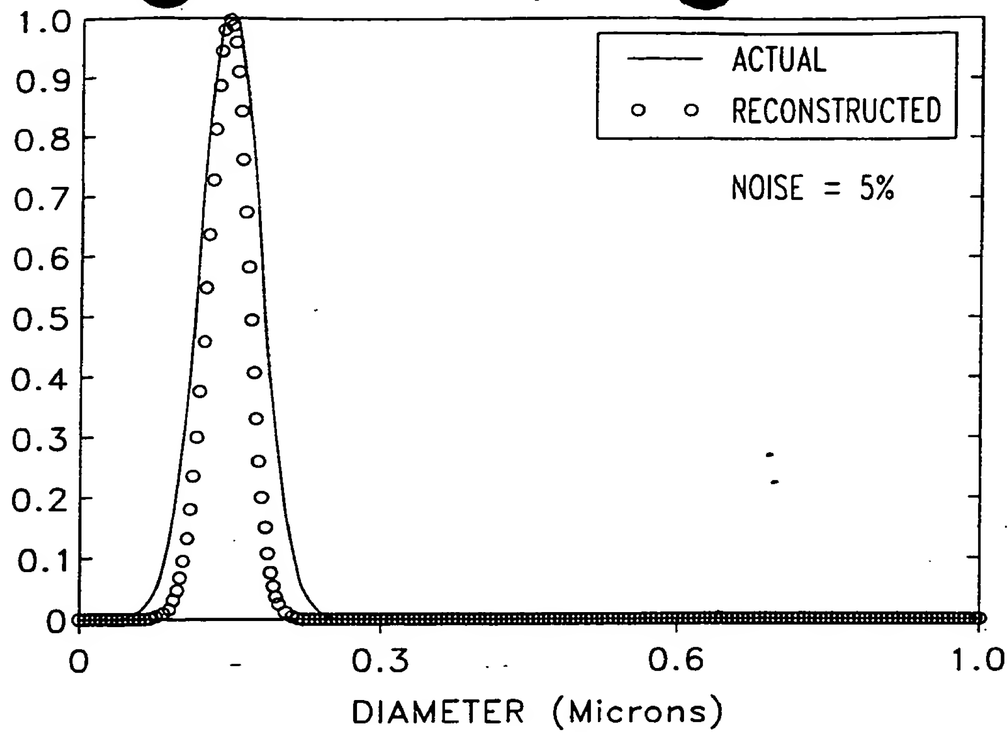
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
ACTUAL
RECONSTRUCTED
NOISE = 5%
0
0.3
0.6
1.0
DIAMETER (Microns)

Fig. 17c

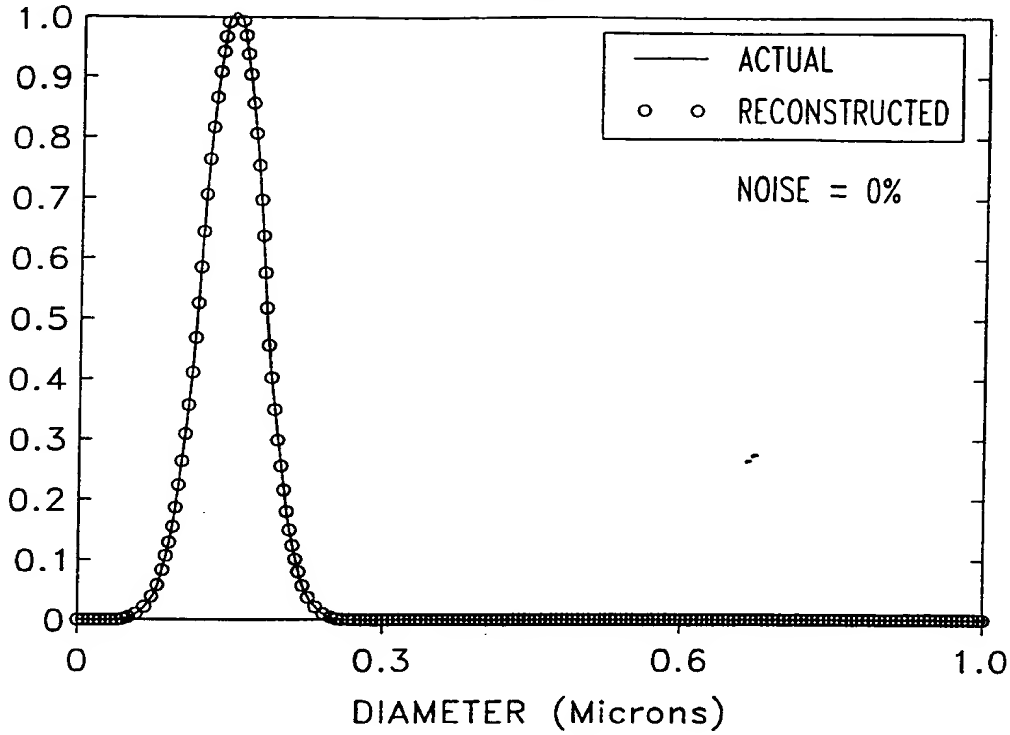

Fig. 17a

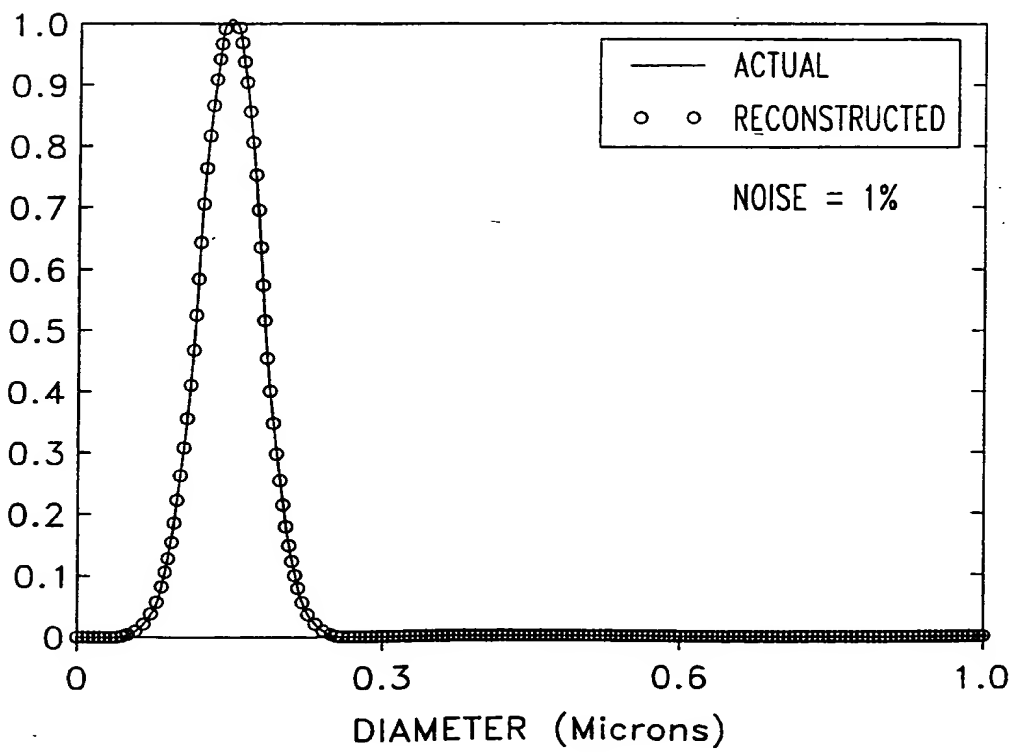

Fig. 17b

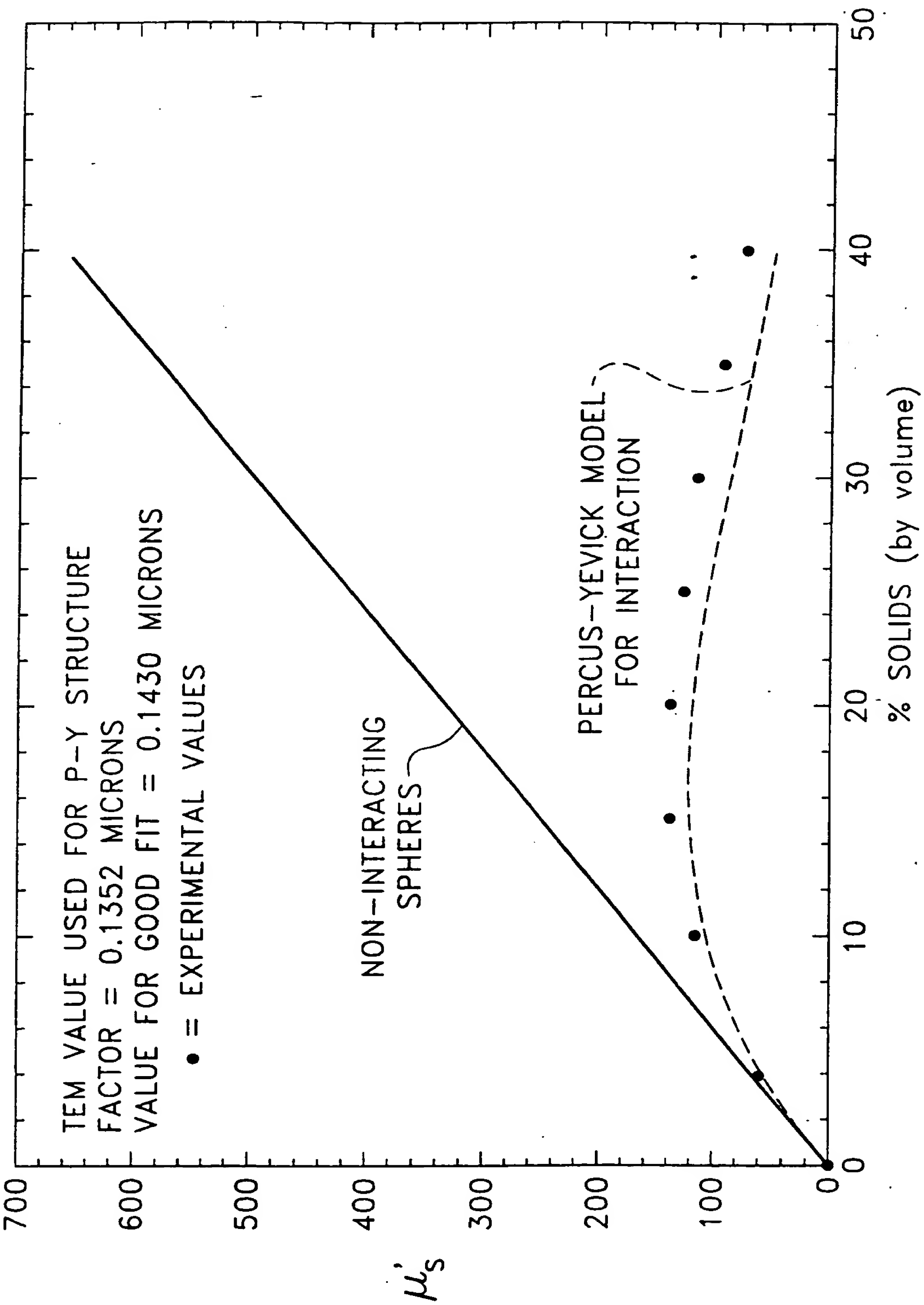
TEM VALUE USED FOR P-Y STRUCTURE
FACTOR = 0.1352 MICRONS
VALUE FOR GOOD FIT = 0.1430 MICRONS
● = EXPERIMENTAL VALUES
NON-INTERACTING
SPHERES
PERCUS-YEVICK MODEL
FOR INTERACTION
700
600
500
400
300
200
100
0
μ's
0
10
20
30
40
50
% SOLIDS (by volume)

Fig. 16c

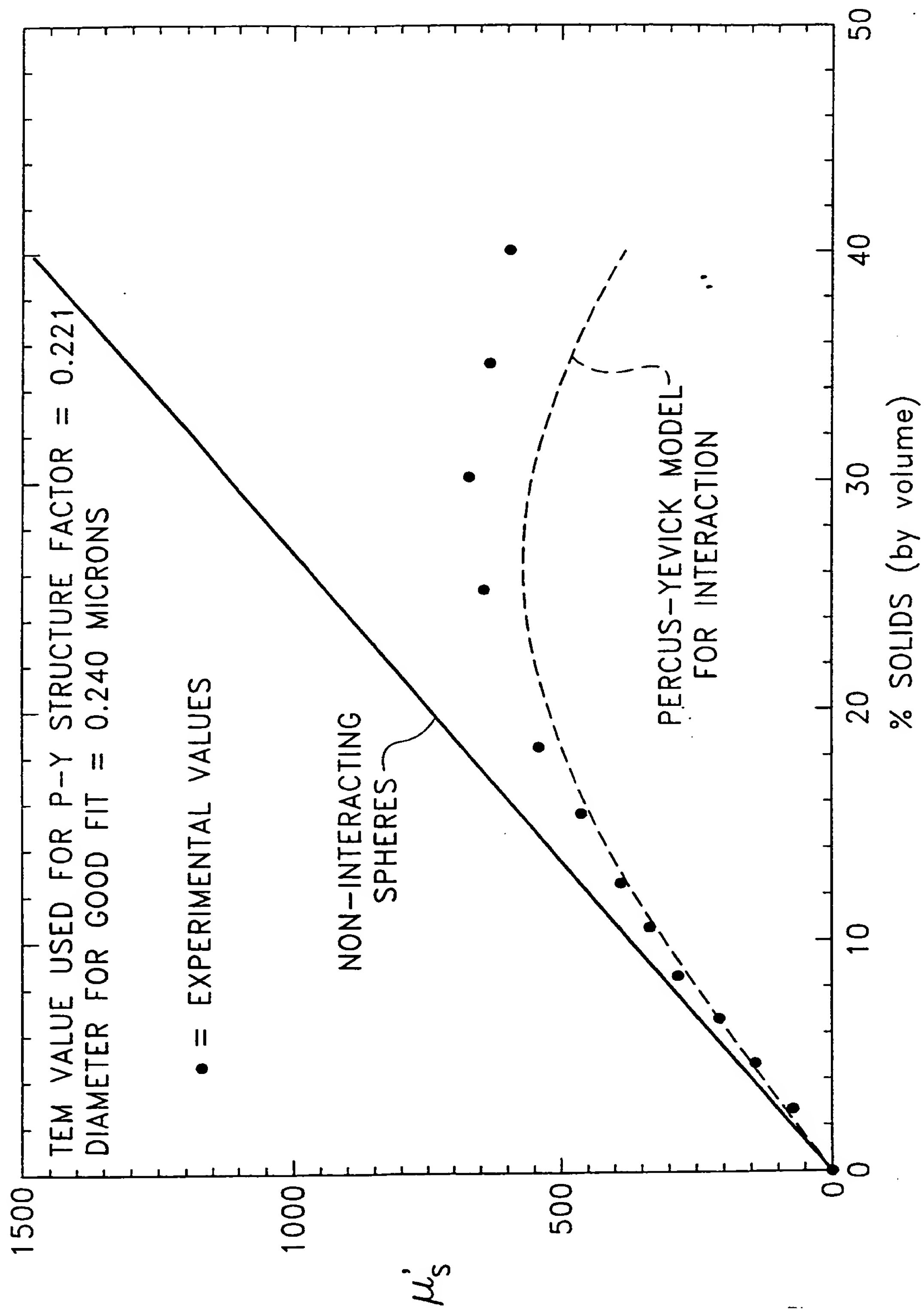
TEM VALUE USED FOR P–Y STRUCTURE FACTOR = 0.221
DIAMETER FOR GOOD FIT = 0.240 MICRONS
● = EXPERIMENTAL VALUES
NON–INTERACTING SPHERES
PERCUS–YEVICK MODEL FOR INTERACTION
1500
1000
500
0
μ_s'
0
10
20
30
40
50
% SOLIDS (by volume)

Fig. 16b

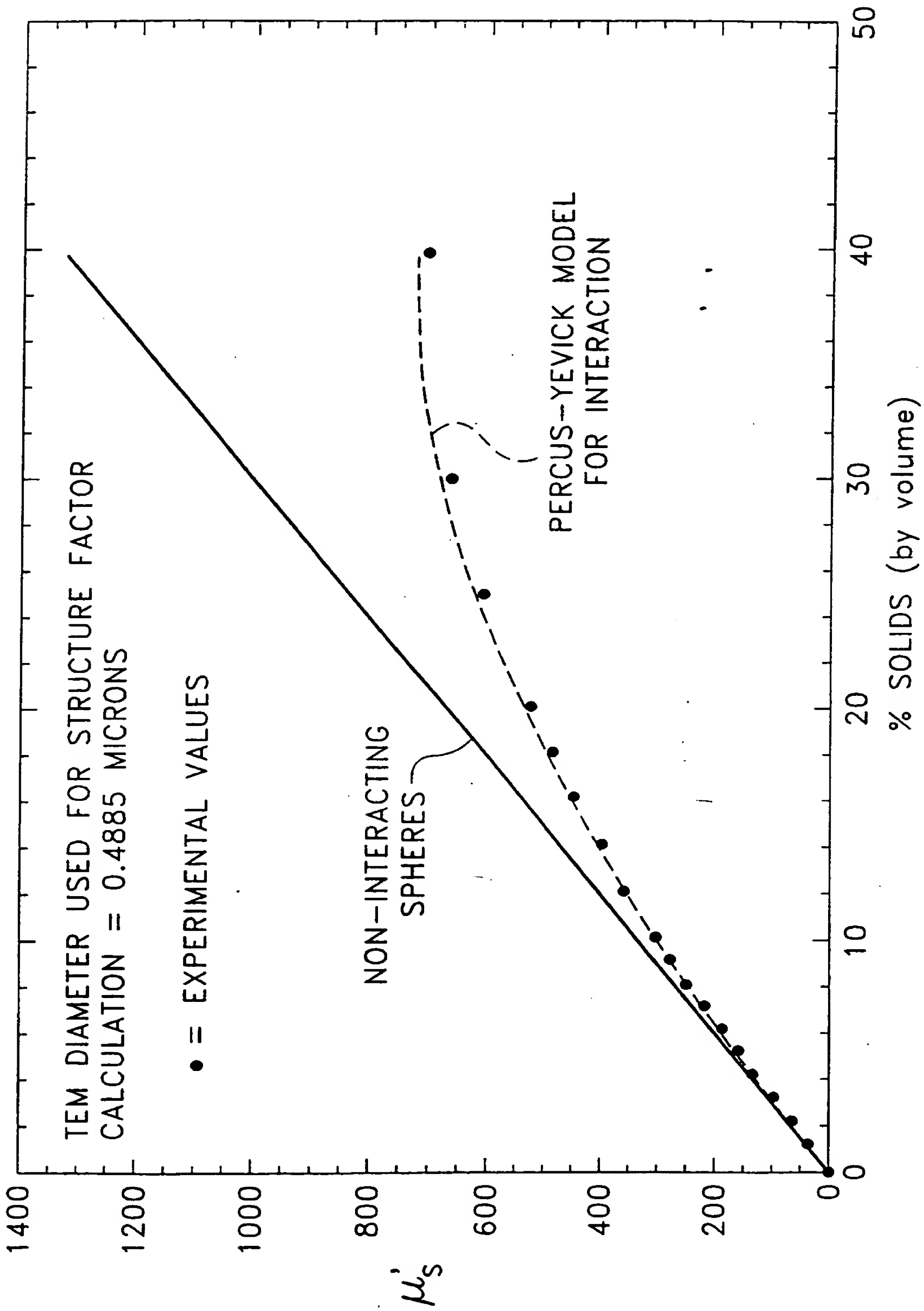
TEM DIAMETER USED FOR STRUCTURE FACTOR
CALCULATION = 0.4885 MICRONS
● = EXPERIMENTAL VALUES
NON-INTERACTING
SPHERES
PERCUS-YEVICK MODEL
FOR INTERACTION
μ_s'
1400
1200
1000
800
600
400
200
0
0
10
20
30
40
50
% SOLIDS (by volume)

Fig. 16a

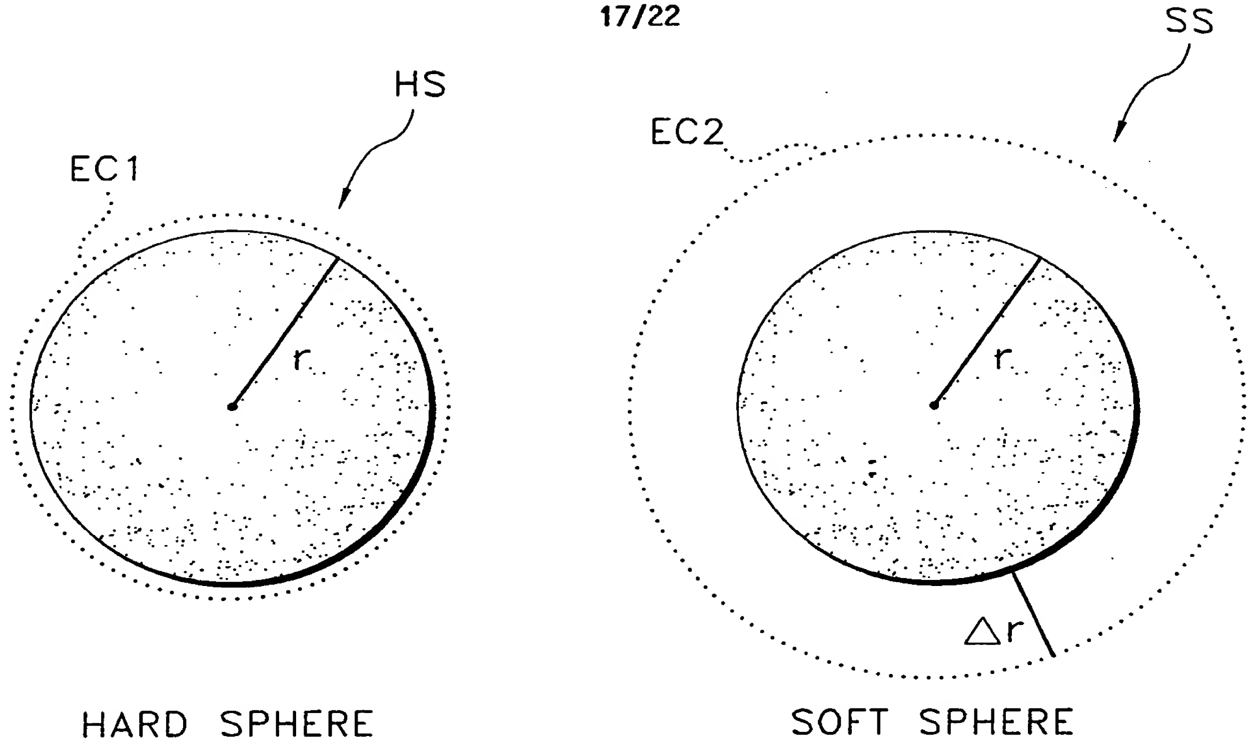
SS
HS
EC2
EC1
r
r
△r
HARD SPHERE
SOFT SPHERE

Fig. 14

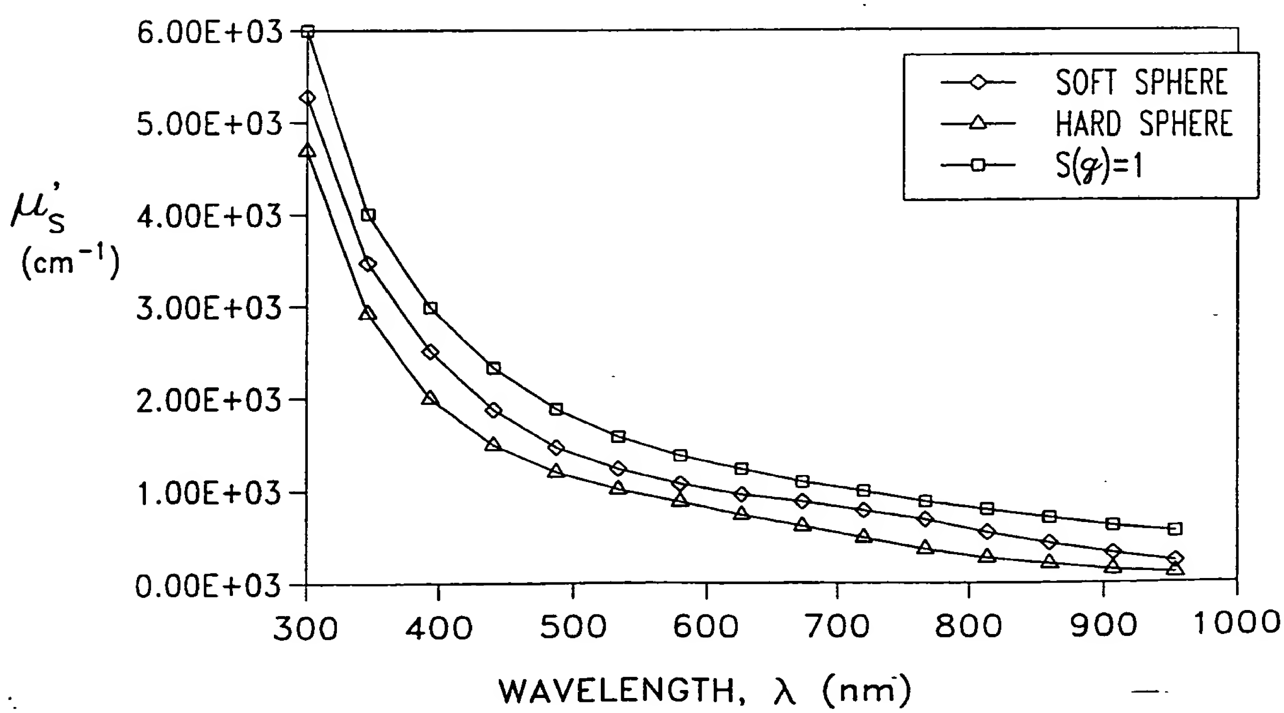
6.00E+03
5.00E+03
4.00E+03
3.00E+03
2.00E+03
1.00E+03
0.00E+03
μ_s' (cm^{-1})
SOFT SPHERE
HARD SPHERE
S(q)=1
300
400
500
600
700
800
900
1000
WAVELENGTH, λ (nm)

Fig. 15

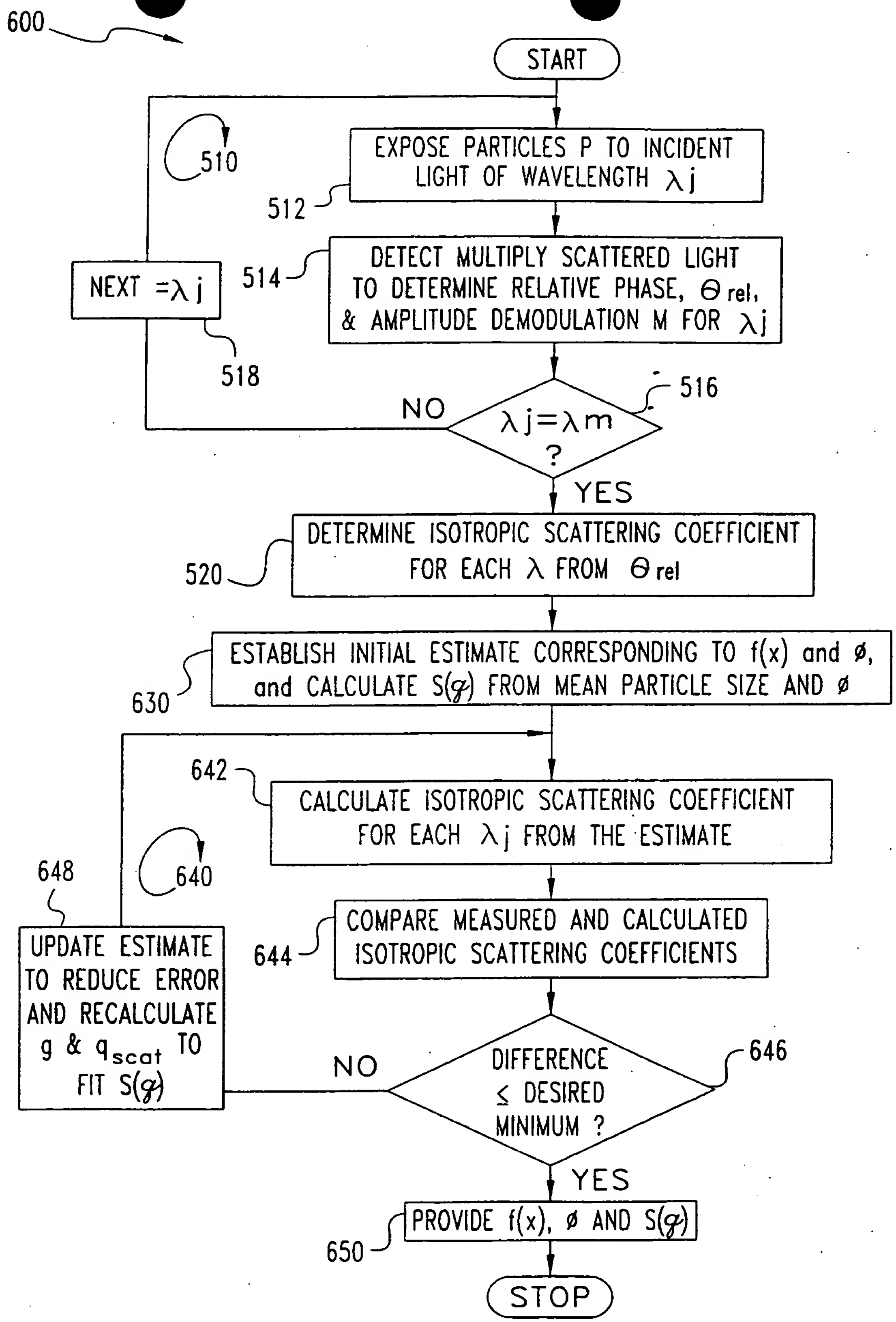
600
START
EXPOSE PARTICLES P TO INCIDENT LIGHT OF WAVELENGTH λj
510
512
DETECT MULTIPLY SCATTERED LIGHT TO DETERMINE RELATIVE PHASE, Θrel, & AMPLITUDE DEMODULATION M FOR λj
514
NEXT =λj
518
516
NO
λj=λm ?
YES
DETERMINE ISOTROPIC SCATTERING COEFFICIENT FOR EACH λ FROM Θrel
520
ESTABLISH INITIAL ESTIMATE CORRESPONDING TO f(x) and ø, and CALCULATE S(q) FROM MEAN PARTICLE SIZE AND ø
630
642
CALCULATE ISOTROPIC SCATTERING COEFFICIENT FOR EACH λj FROM THE ESTIMATE
648
640
UPDATE ESTIMATE TO REDUCE ERROR AND RECALCULATE g & qscat TO FIT S(q)
COMPARE MEASURED AND CALCULATED ISOTROPIC SCATTERING COEFFICIENTS
644
NO
DIFFERENCE ≤ DESIRED MINIMUM ?
646
YES
PROVIDE f(x), ø AND S(q)
650
STOP

Fig. 13

Titanium Dioxide Suspension, S2

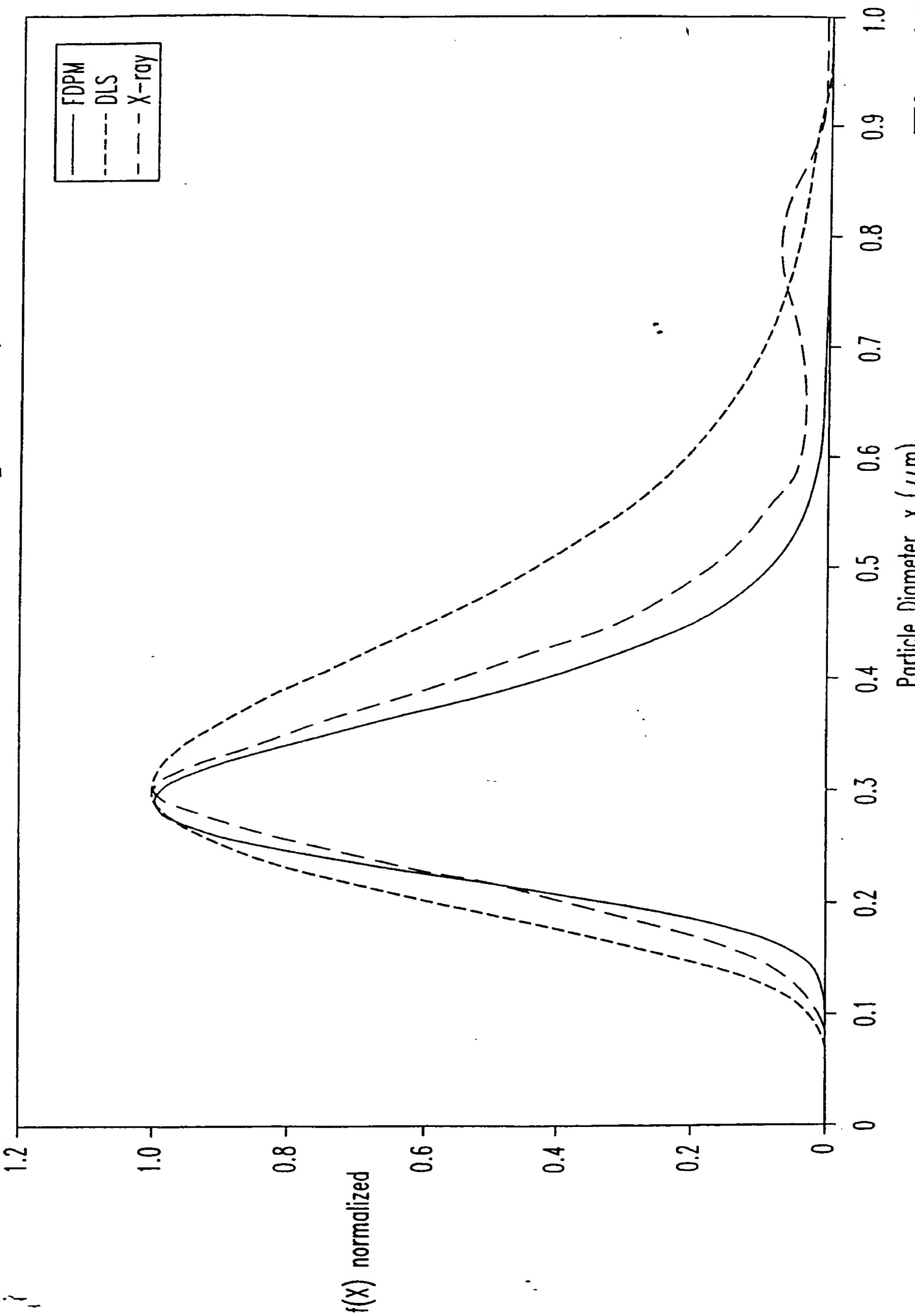

Fig. 12b

Titanium Dioxide Suspension, S1

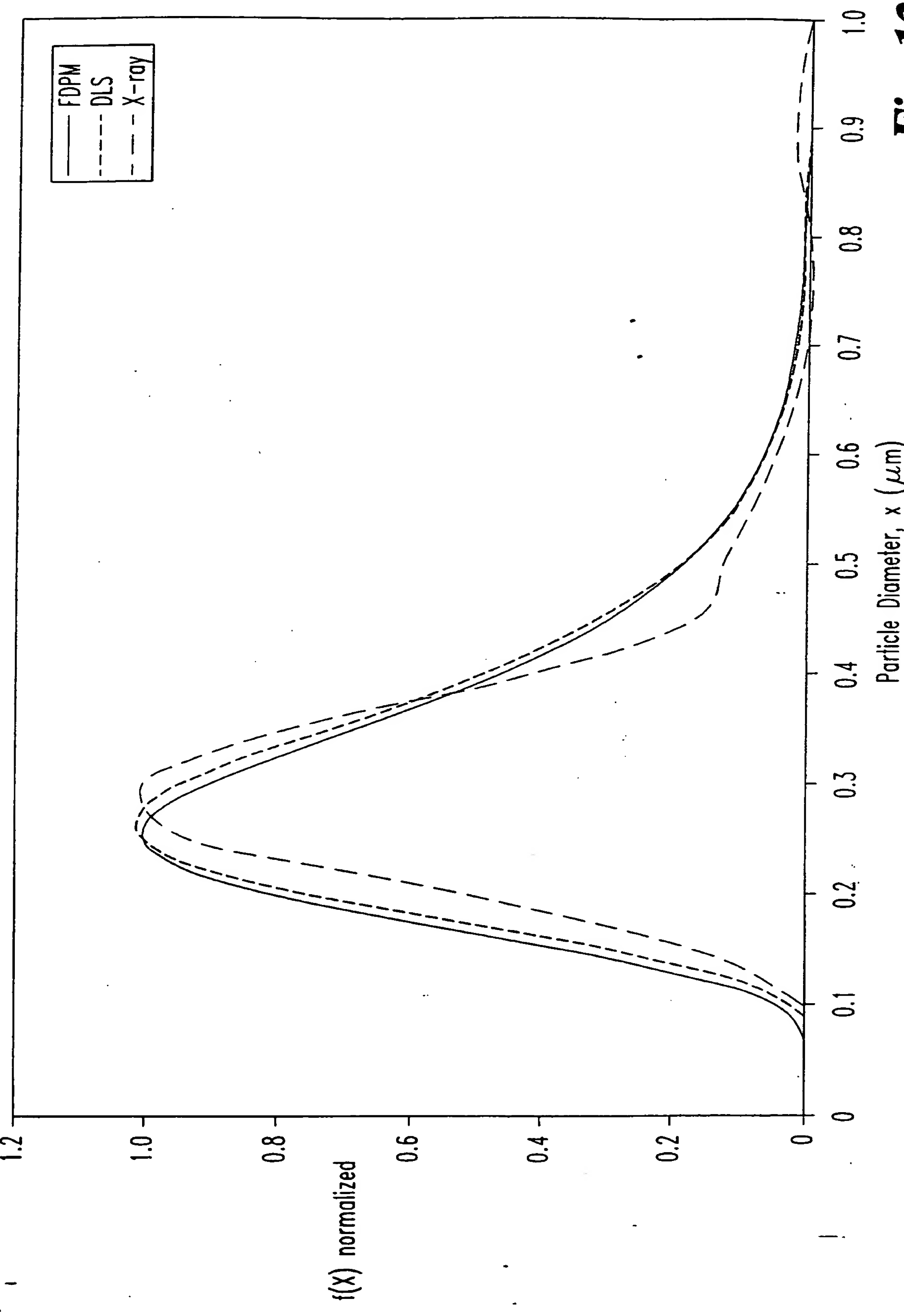

Fig. 12a

TiO_2 PSD Determination

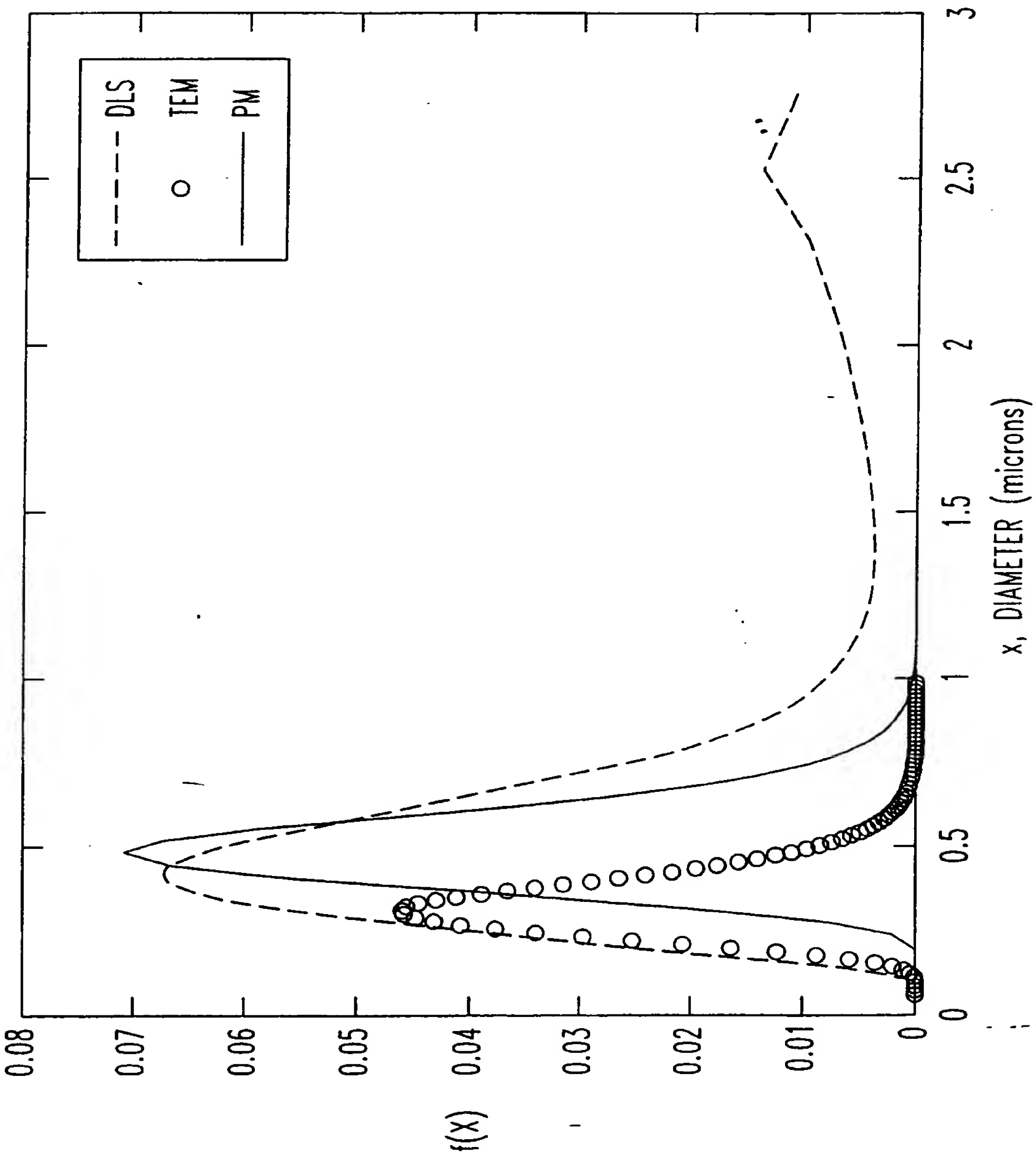

Fig. 12

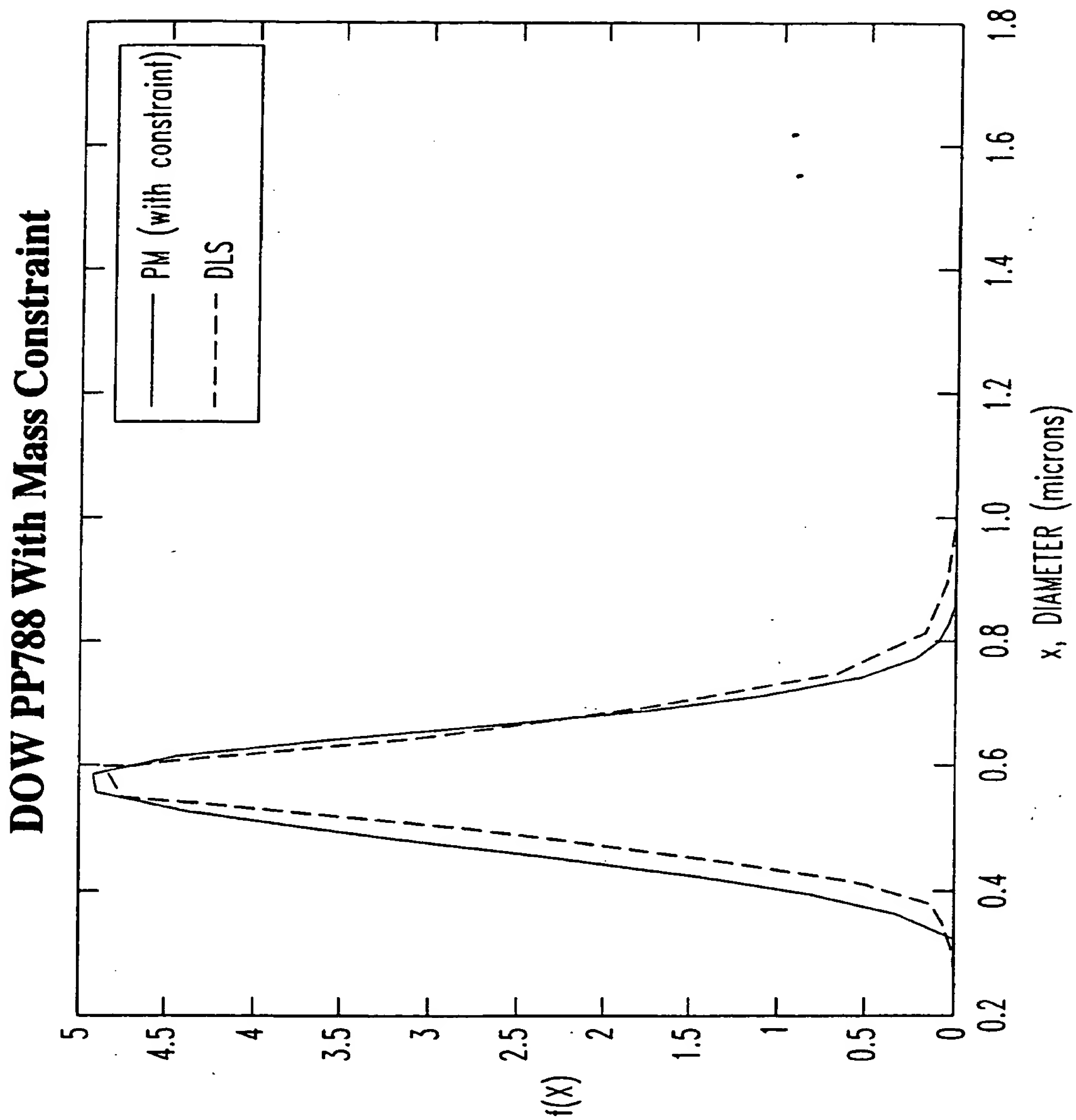
DOW PP788 With Mass Constraint
PM (with constraint)
DLS
f(X)
x, DIAMETER (microns)
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5

Fig. 11

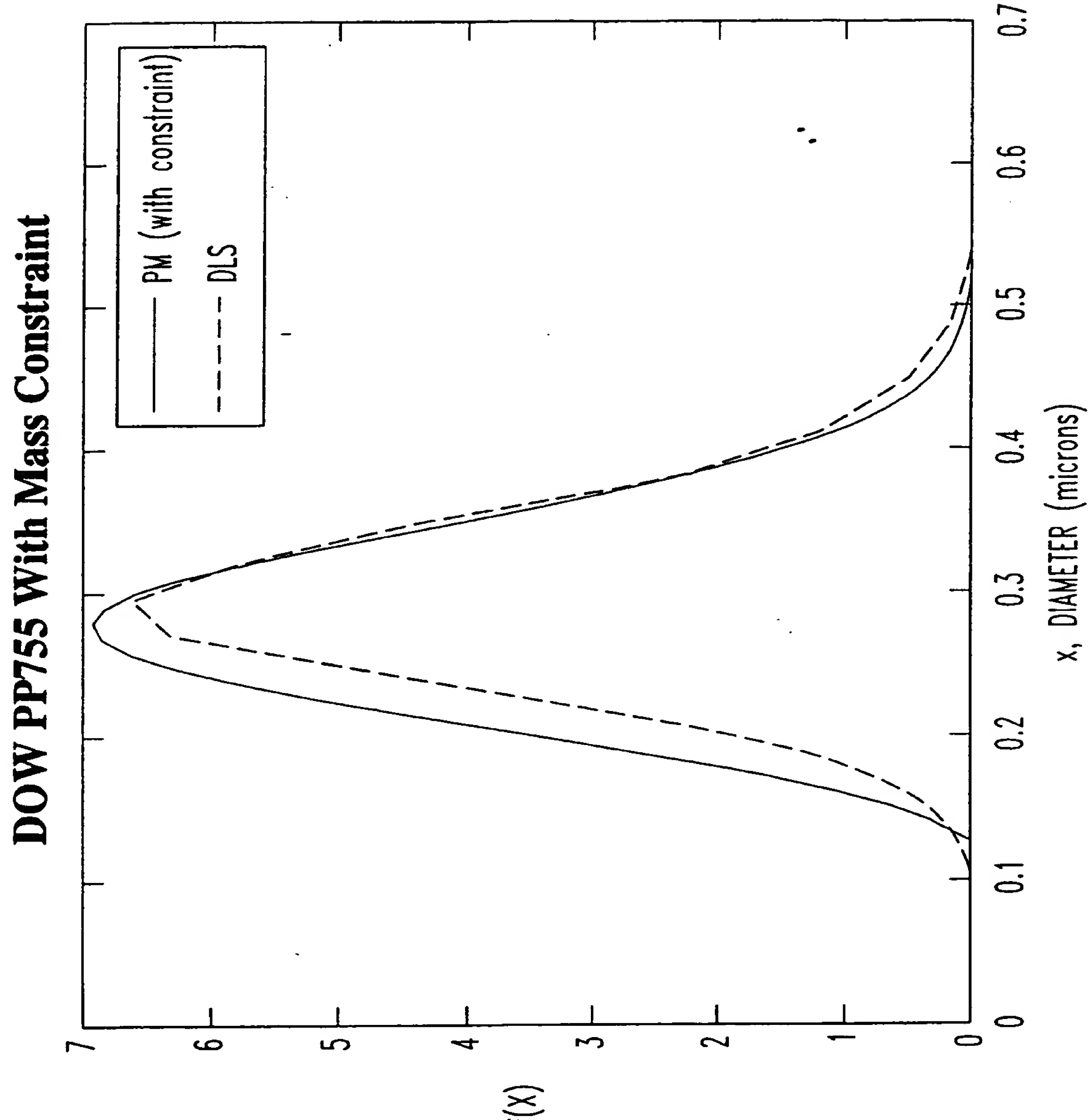
DOW PP755 With Mass Constraint
PM (with constraint)
DLS
f(X)
x, DIAMETER (microns)
0
1
2
3
4
5
6
7
0.1
0.2
0.3
0.4
0.5
0.6
0.7

Fig. 10

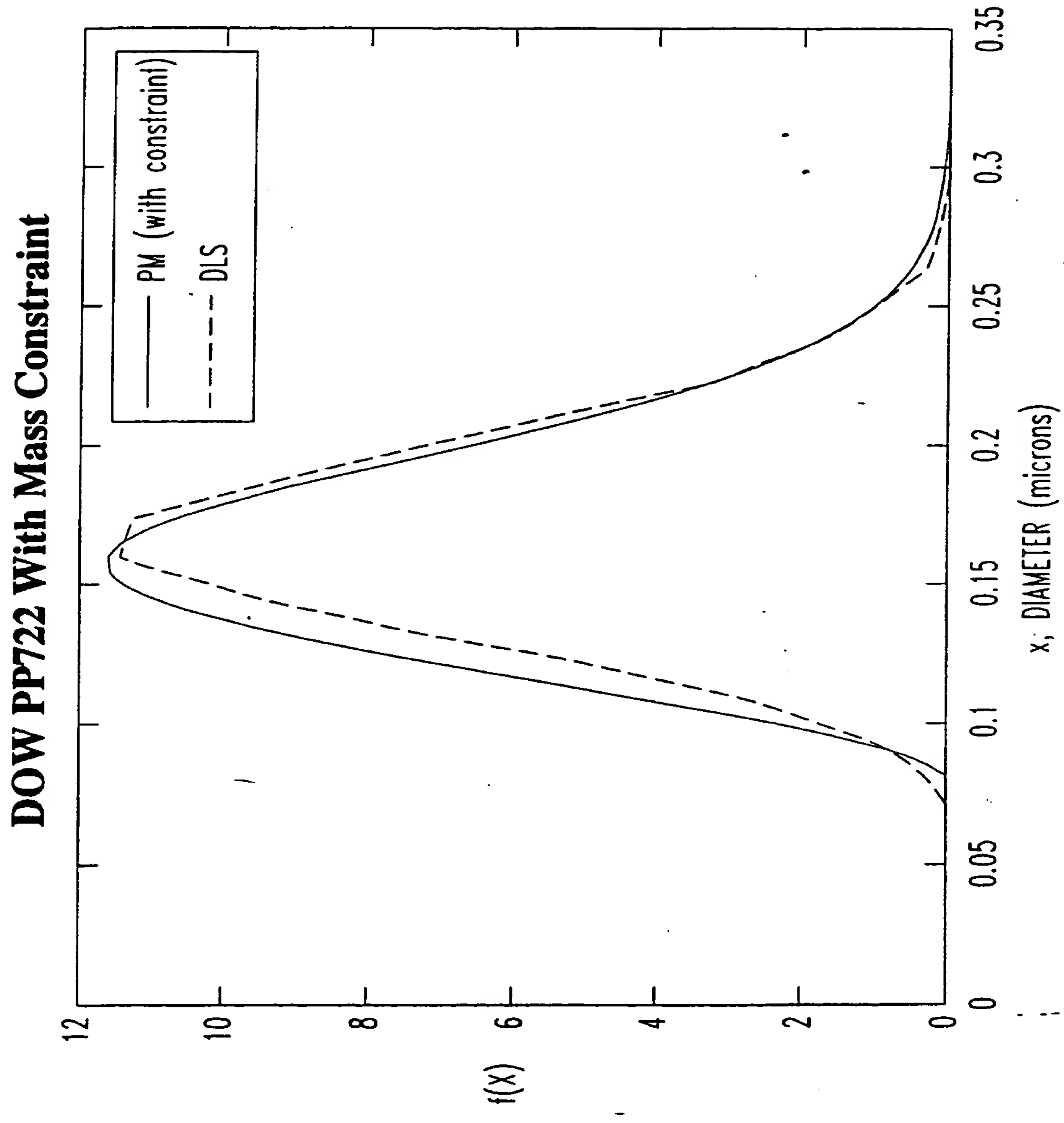
DOW PP722 With Mass Constraint
PM (with constraint)
DLS
f(X)
x; DIAMETER (microns)
0
2
4
6
8
10
12
0.05
0.1
0.15
0.2
0.25
0.3
0.35

Fig. 9

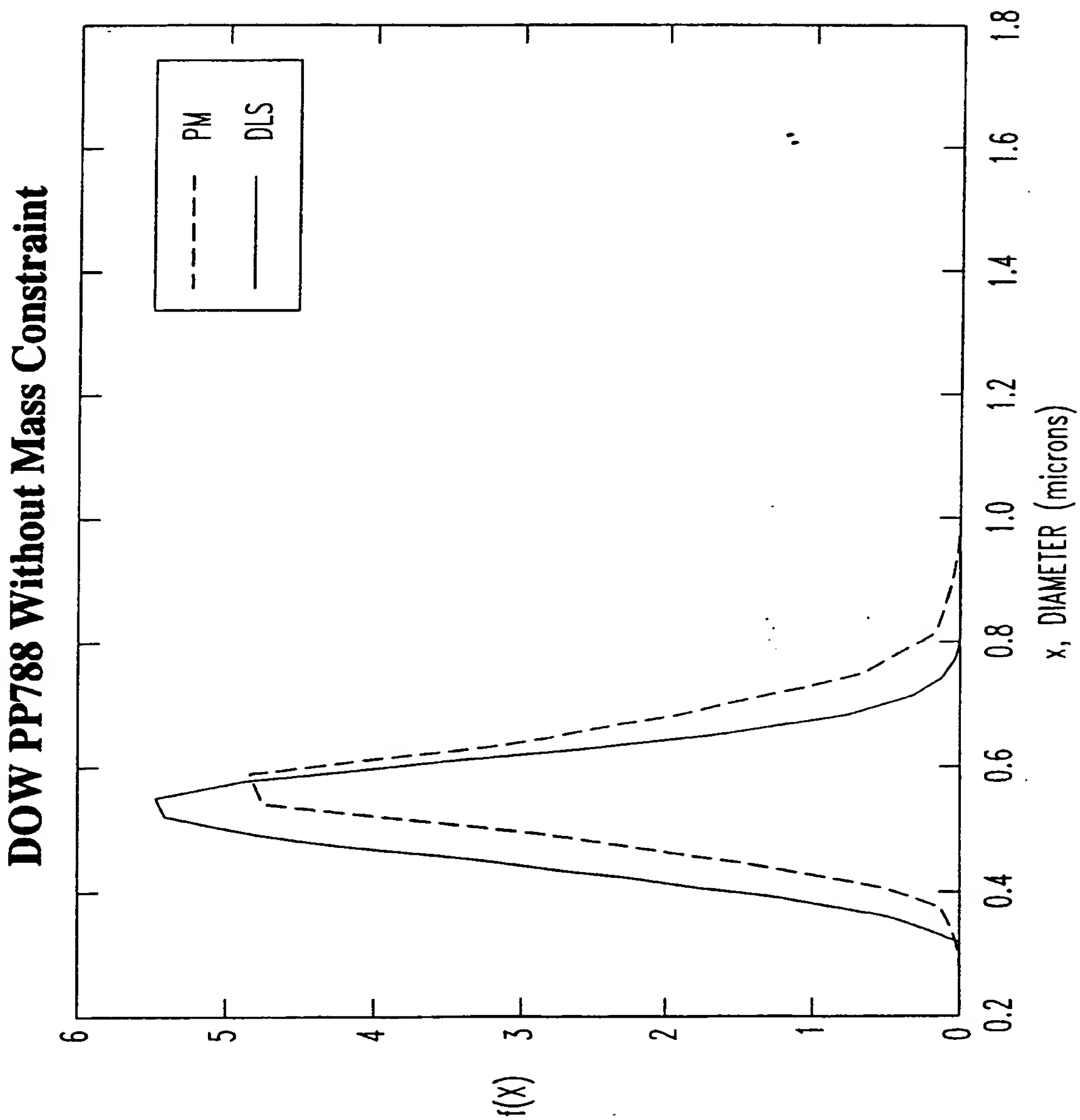
DOW PP788 Without Mass Constraint
PM
DLS
f(X)
0
1
2
3
4
5
6
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
x, DIAMETER (microns)

Fig. 8

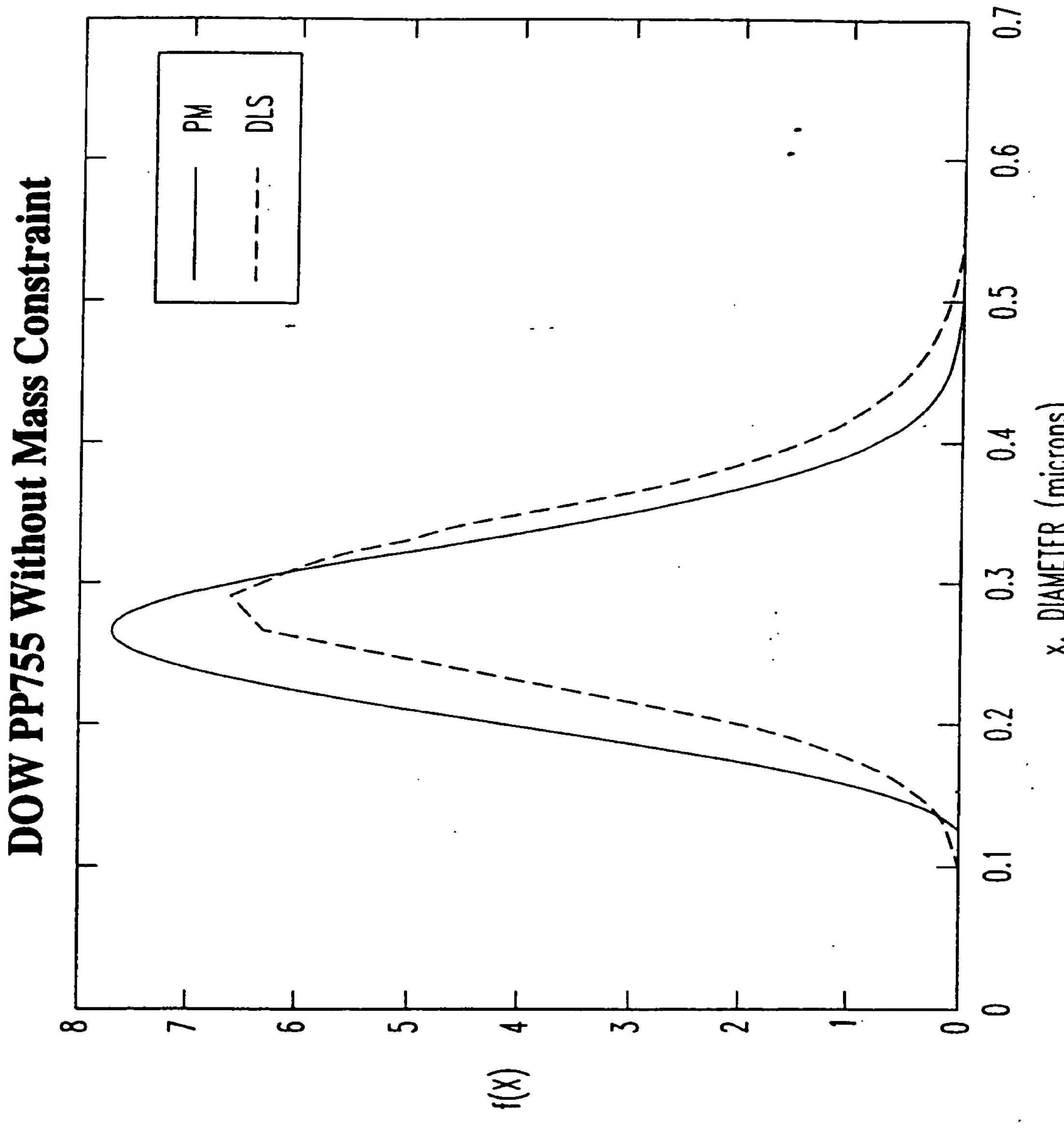
DOW PP755 Without Mass Constraint
PM
DLS
f(X)
x, DIAMETER (microns)
0
1
2
3
4
5
6
7
8
0.1
0.2
0.3
0.4
0.5
0.6
0.7

Fig. 7

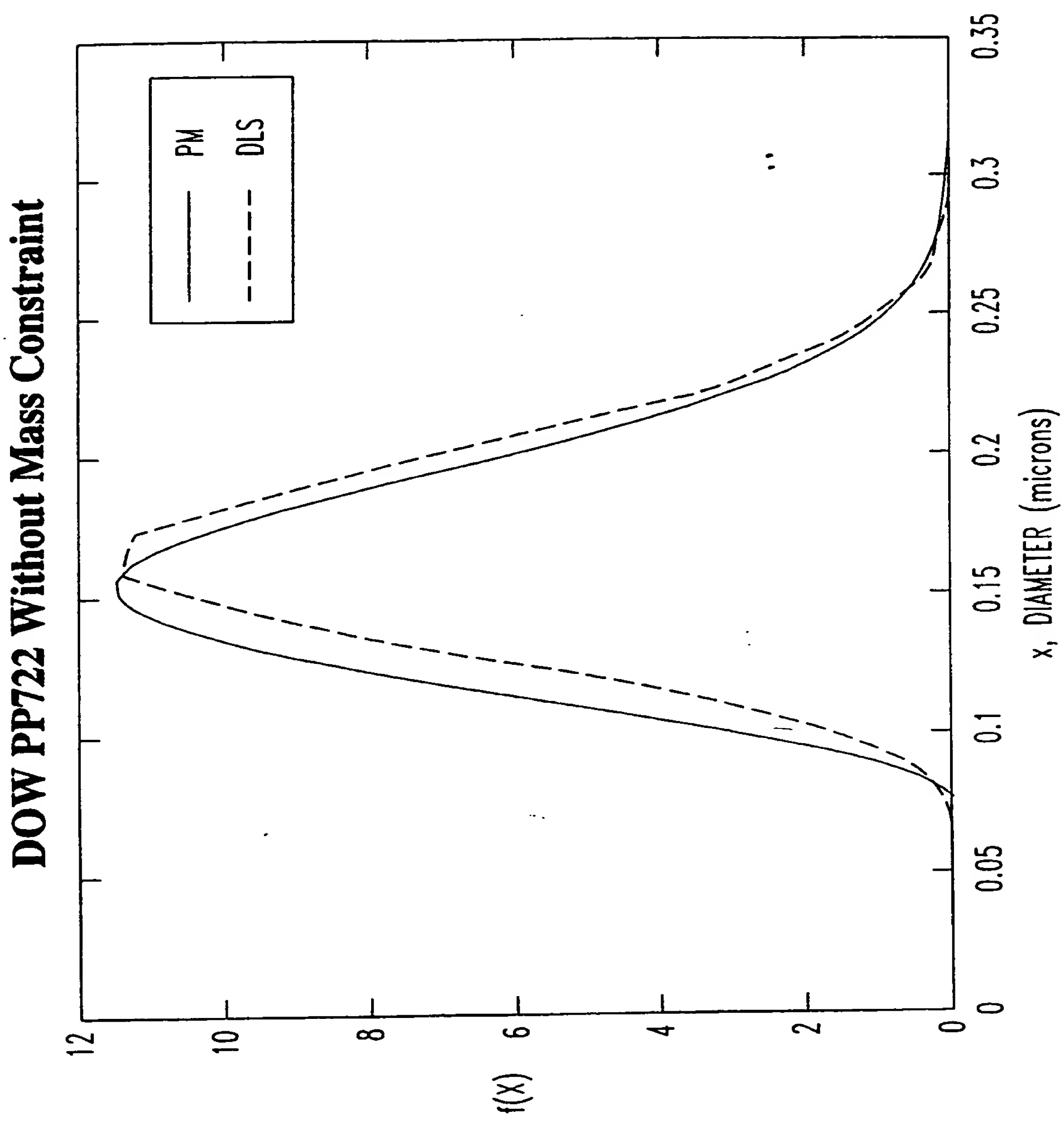
DOW PP722 Without Mass Constraint
PM
DLS
f(X)
0
2
4
6
8
10
12
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
x, DIAMETER (microns)

Fig. 6

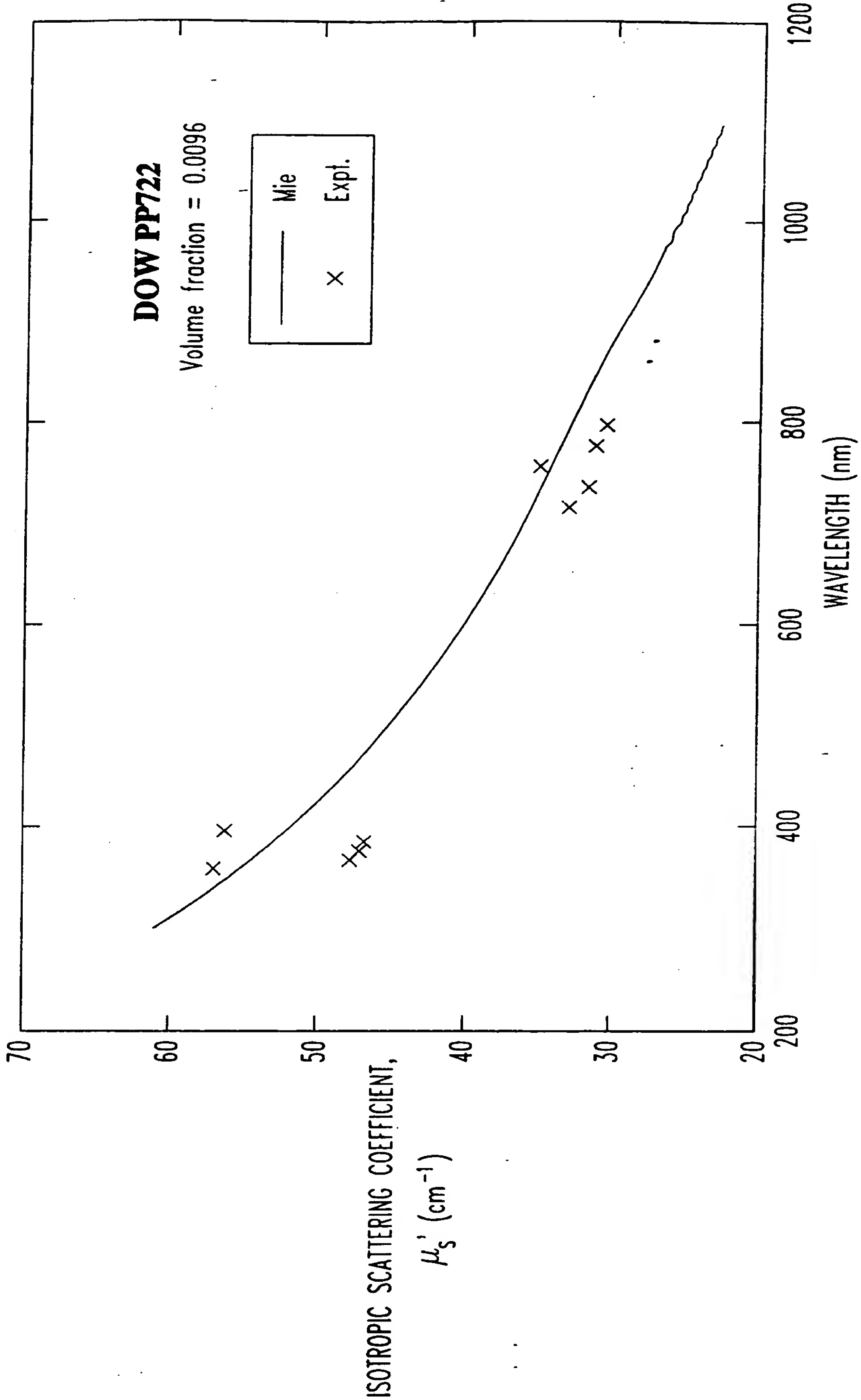
DOW PP722
Volume fraction = 0.0096
Mie
Expt.
ISOTROPIC SCATTERING COEFFICIENT,
μ_s' (cm^{-1})
70
60
50
40
30
20
200
400
600
800
1000
1200
WAVELENGTH (nm)

Fig. 5

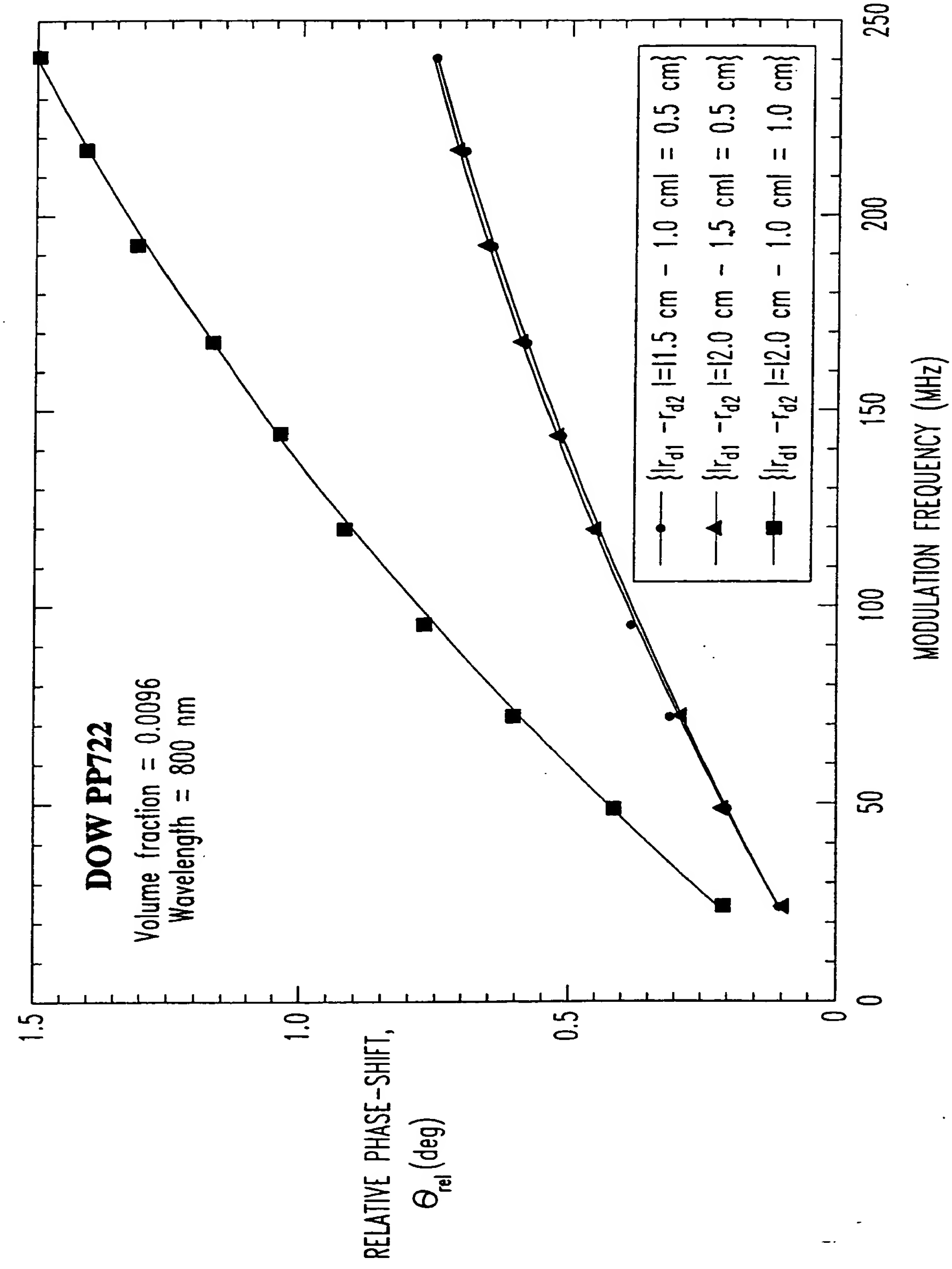
DOW PP722
Volume fraction = 0.0096
Wavelength = 800 nm
{|r_d1 - r_d2 |=|1.5 cm - 1.0 cm| = 0.5 cm}
{|r_d1 - r_d2 |=|2.0 cm - 1.5 cm| = 0.5 cm}
{|r_d1 - r_d2 |=|2.0 cm - 1.0 cm| = 1.0 cm}
RELATIVE PHASE-SHIFT,
Θ_rel (deg)
MODULATION FREQUENCY (MHz)
0
0.5
1.0
1.5
0
50
100
150
200
250

Fig. 4

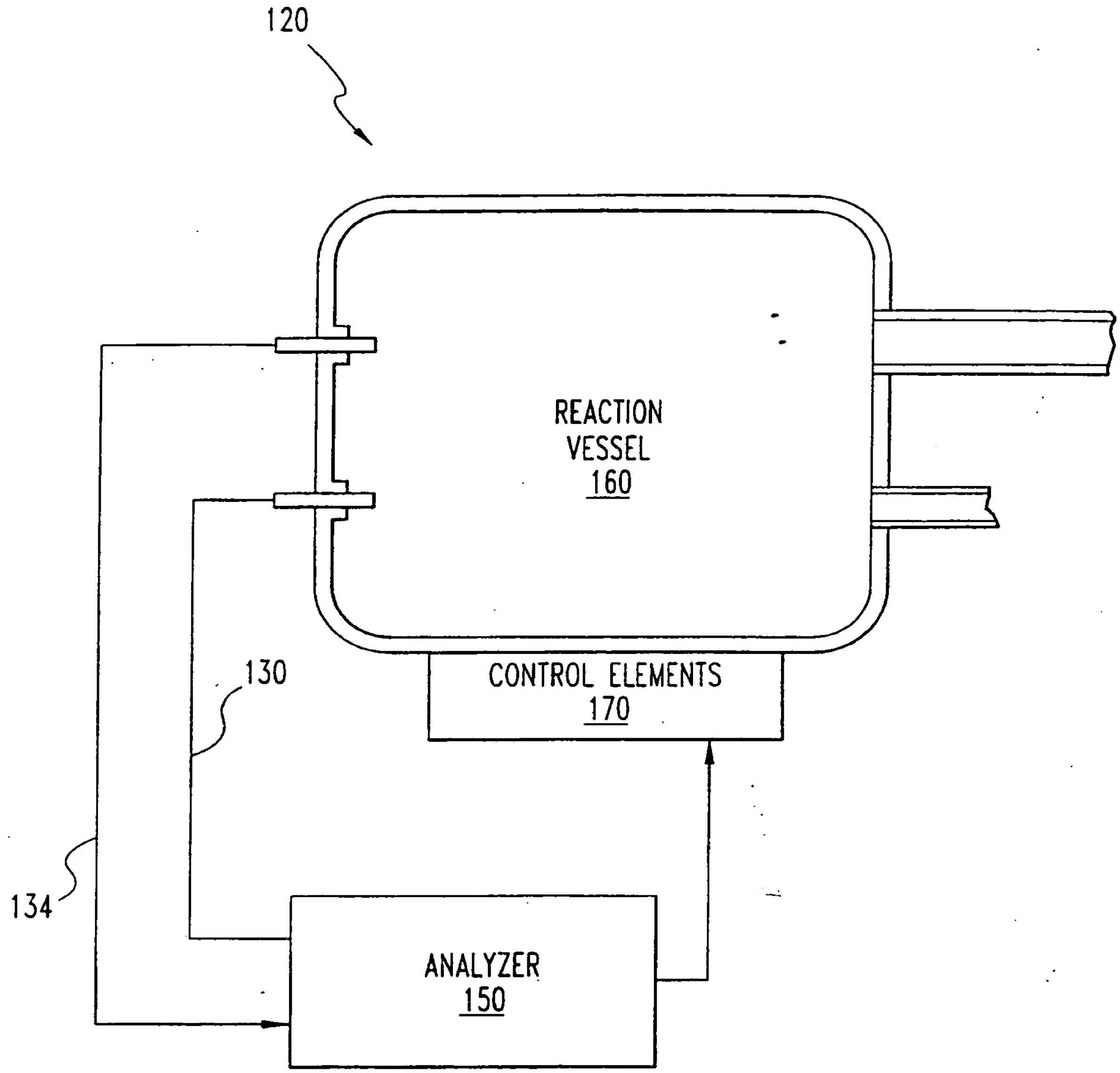
120
REACTION
VESSEL
160
CONTROL ELEMENTS
170
130
134
ANALYZER
150

Fig. 3

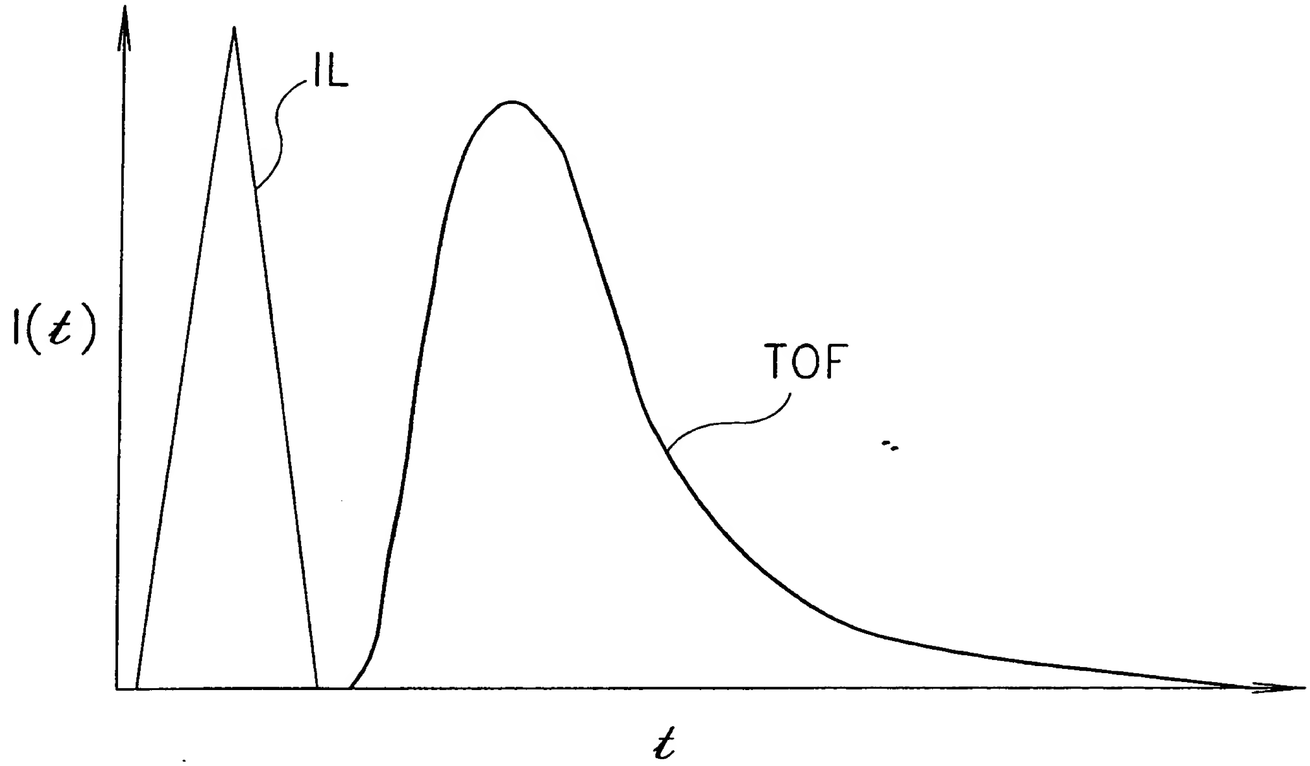

Fig. 2a

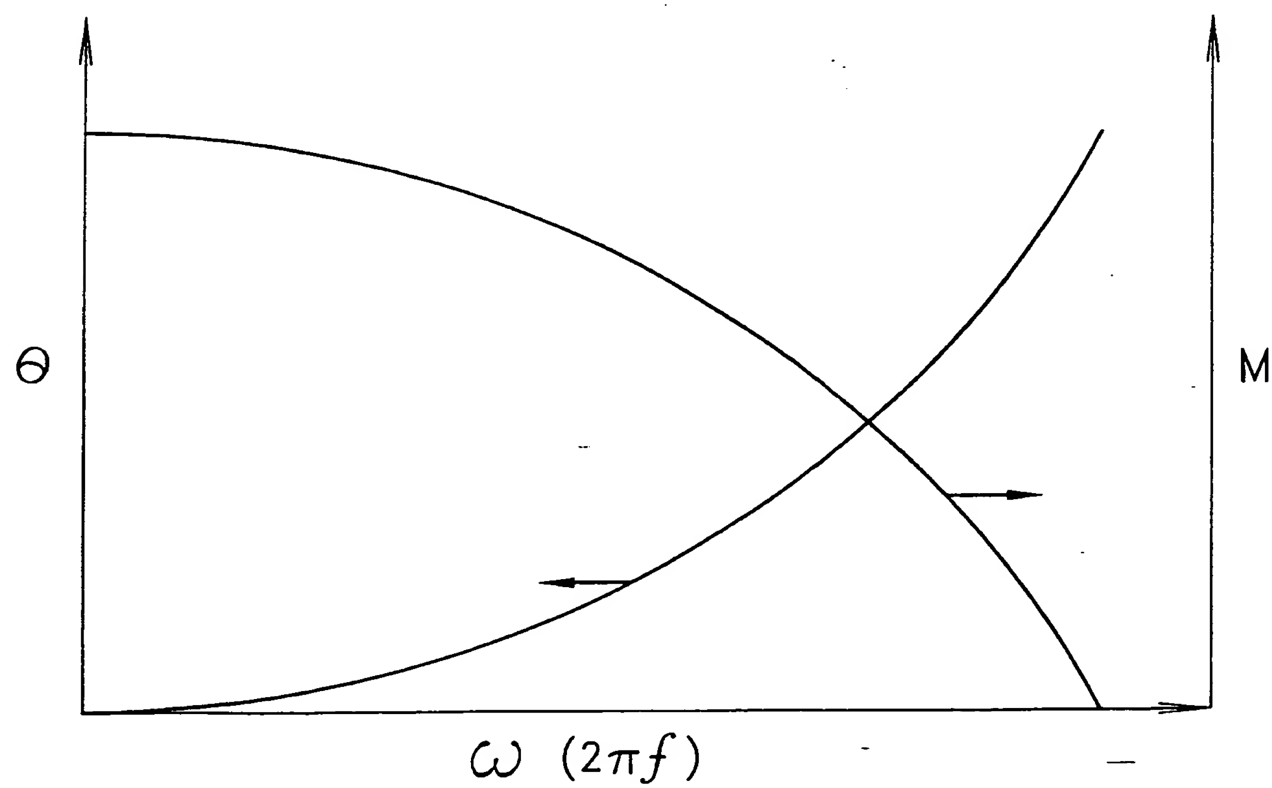

Fig. 2b

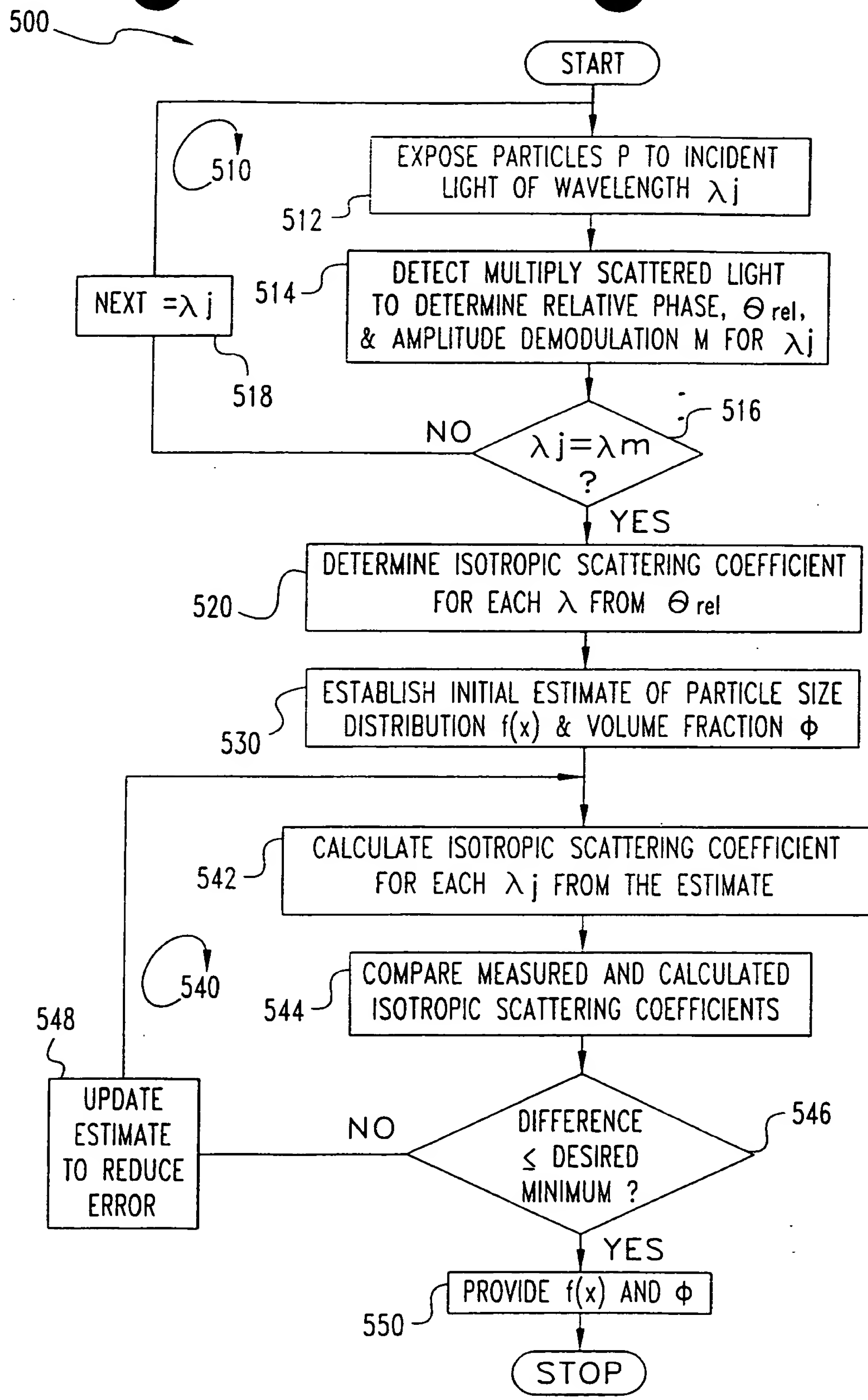
500
START
510
EXPOSE PARTICLES P TO INCIDENT LIGHT OF WAVELENGTH λj
512
NEXT =λj
518
514
DETECT MULTIPLY SCATTERED LIGHT TO DETERMINE RELATIVE PHASE, Θ rel, & AMPLITUDE DEMODULATION M FOR λj
516
NO
λj=λm ?
YES
520
DETERMINE ISOTROPIC SCATTERING COEFFICIENT FOR EACH λ FROM Θ rel
530
ESTABLISH INITIAL ESTIMATE OF PARTICLE SIZE DISTRIBUTION f(x) & VOLUME FRACTION Φ
542
CALCULATE ISOTROPIC SCATTERING COEFFICIENT FOR EACH λj FROM THE ESTIMATE
540
548
544
COMPARE MEASURED AND CALCULATED ISOTROPIC SCATTERING COEFFICIENTS
UPDATE ESTIMATE TO REDUCE ERROR
NO
DIFFERENCE ≤ DESIRED MINIMUM ?
546
YES
550
PROVIDE f(x) AND Φ
STOP

Fig. 2

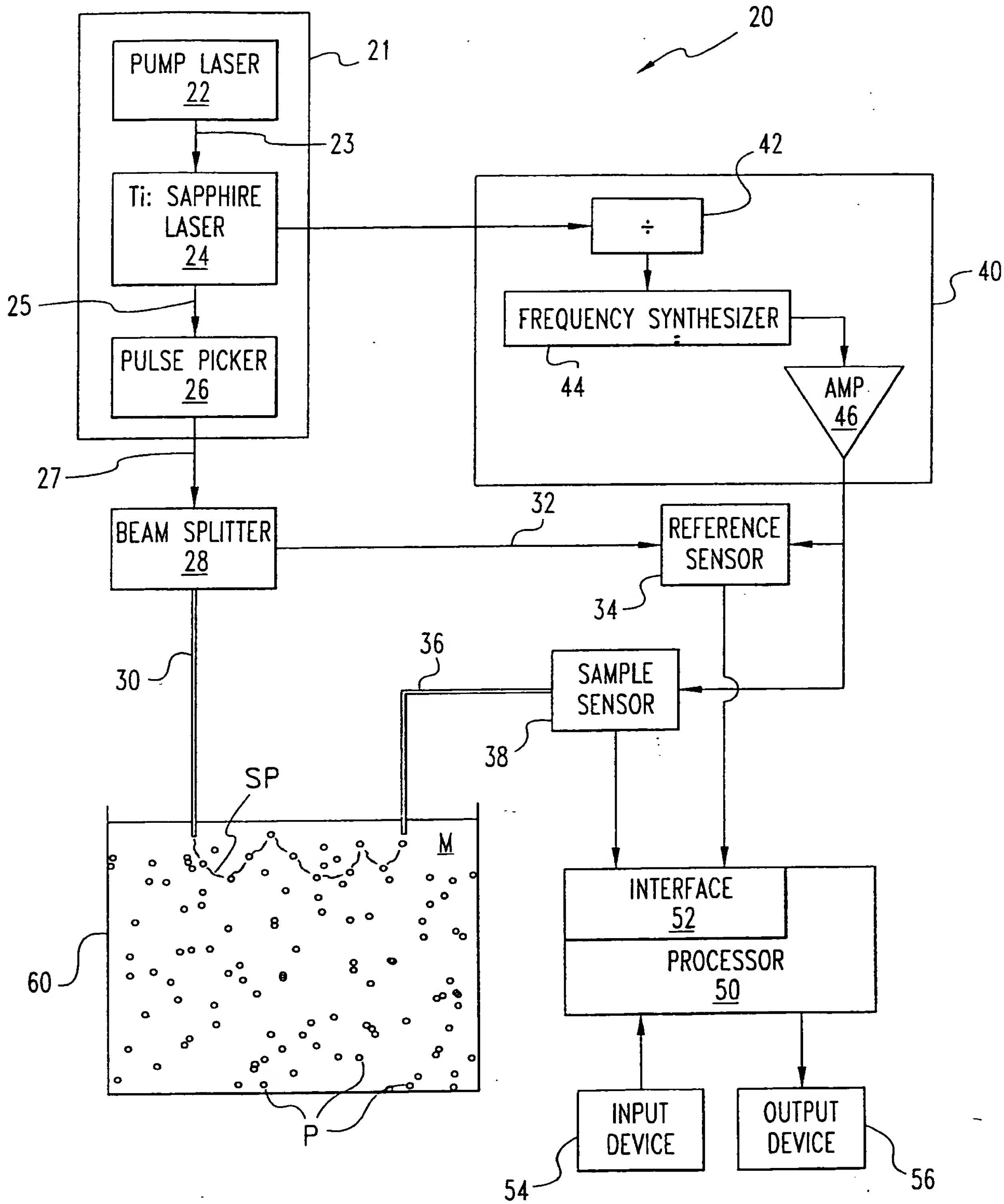
20
21
PUMP LASER 22
23
Ti: SAPPHIRE LASER 24
25
PULSE PICKER 26
27
42
÷
40
FREQUENCY SYNTHESIZER
44
AMP 46
BEAM SPLITTER 28
32
REFERENCE SENSOR
34
30
36
SAMPLE SENSOR
38
SP
M
60
P
INTERFACE 52
PROCESSOR 50
INPUT DEVICE
54
OUTPUT DEVICE
56

Fig. 1

droplets dispersed in a fluid medium, the droplets and the medium having different indices of refraction.

(d) determining a calculated isotropic scattering coefficient for each of the wavelengths from an estimate of at least one of particle size distribution or particle volume fraction;

(e) comparing the observed isotropic scattering coefficient and calculated isotropic scattering coefficient for each of the wavelengths to establish and error;

(f) adjusting the estimate and repeating said determining and said comparing until the error reaches a desired minimum; and

(g) providing an output corresponding to at least one of the particle size distribution, particle volume fraction, or a particle interaction parameter.

47. The method of claim 46, wherein said determining includes establishing the particle interaction parameter as a function of the particle volume fraction and the particle size distribution.

48. The method of claim 47, wherein the particle interaction parameter corresponds to the P-Y hard sphere structure factor.

49. The method of claim 48, wherein the calculated isotropic scattering coefficient is determined with an equation having the structure factor and an estimated product of the size distribution and the volume fraction as arguments.

50. The method of claim 46, wherein the particles include liquid

function of mass of the particles.

43. The system of claim 41, further comprising a second sensor providing a second detection signal, said scattering signals being determined as a function of said first and second detection signals for each of the wavelengths.

44. The system of claim 41, wherein said structure factor corresponds to a P-Y hard sphere structure factor model.

45. The system of claim 41, wherein said processor further generates an absorption signal corresponding to an absorption coefficient of the medium and determines said absorption signal from said propagation signal.

46. A method of particle analysis, comprising:

(a) exposing a number of particles to a number of light wavelengths of predetermined time-varying intensity;

(b) detecting multiply scattered light from the particles in response to said exposing to determine a number of time-based propagation characteristics of the particles each corresponding to a different one of the wavelengths; and

(c) calculating an observed isotropic scattering coefficient for each of the wavelengths from the characteristics;

different predetermined wavelengths of incident light each having a predetermined time-varying intensity;

a first sensor spaced apart from said source, said first sensor being configured to provide a first detection signal corresponding to detected light, the detected light being multiply scattered by the particles;

a processor responsive to said first detection signal and being configured to receive an exposure signal corresponding to said incident light, said processor being configured to generate: (a) a number of propagation signals by comparing said first detection signal and said exposure signal for each of said wavelengths, said propagation signals each characterizing time of flight of the detected light through the medium resulting from multiple scattering by the particles for a corresponding one of said wavelengths, (b) a number of scattering signals each corresponding to an isotropic scattering coefficient of the medium and being determined from a corresponding one of said propagation signals, and (c) an output signal indicative of at least one of size distribution or volume fraction of the particles, said output signal being determined from said scattering signals and a structure factor, said structure factor accounting for particle-to-particle interactions influencing light scattering behavior of the particles; and

an output device responsive to said output signal to provide an output corresponding to said size distribution or said volume fraction of the particles.

42. The system of claim 41, wherein said processor is further configured to determine said size distribution or said volume fraction as a

calculating a number corresponding to the isotropic scattering coefficient as a function of an estimate of the volume fraction and the size distribution.

37. The method of claim 32, wherein the incident light is intensity modulated at a predetermined frequency, and said determining includes comparing the incident light and the scattered light to determine the value, and the value is representative of a relative phase or amplitude of the scattered light for the predetermined frequency.

38. The method of claim 37, wherein said detecting includes detecting the scattered light with a second sensor spaced apart from the first sensor by a separation distance and said determining includes calculating the quantity in accordance with the separation distance.

39. The method of claim 37, wherein said providing includes determining the volume fraction or size distribution in accordance with the diffusion equation for multiply scattered light.

40. The method of claim 32, wherein the particle interaction parameter is determined from a P-Y structure factor model.

41. A system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light, comprising:

a light source configured to expose the medium to a number of

(b) detecting multiply scattered light in response to said exposing to determine a time-based value characteristic of propagation time of the multiply scattered light through the fluid;

(c) determining a quantity as a function of the value, the quantity corresponding to an isotropic scattering coefficient; and

(d) providing an output determined from the quantity, the output corresponding to at least one of particle volume fraction, particle size distribution, or a particle interaction parameter, the particle interaction parameter corresponding to particle-to-particle interactions influencing light scattering behavior of the particles.

33. The method of claim 32, further comprising controlling a process in which the particles are altered by utilizing the output as a feedback variable.

34. The method of claim 32, wherein said providing includes establishing an estimate corresponding to volume fraction and the size distribution and determining the particle interaction parameter as a function of the estimate.

35. The method of claim 34, further comprising constraining the estimate to maintain mass balance.

36. The method of claim 32, wherein said providing includes

corresponding to a nonlinear relationship between particle concentration and an isotropic scattering coefficient for the particles.

27. The method of claim 26, wherein the particles are suspended in a fluid medium and further comprising controlling a process in accordance with the output.

28. The method of claim 26, wherein the particles have a concentration in the fluid medium of at least about 10% by volume.

29. The method of claim 26, wherein said determining includes calculating at least one of volume fraction and size distribution of the particles in the fluid.

30. The method of claim 26, wherein the particle interaction parameter is determined from the Percus-Yevick hard sphere model.

31. The method of claim 30, wherein said calculating includes adjusting the hard sphere model to account for forces between the particles.

32. A method of analysis, comprising:

(a) exposing a fluid to an incident light, the fluid having a number of suspended particles therein, the suspended particles being sufficiently concentrated in the fluid to scatter light;

error reaches a desired minimum.

23. The method of claim 22, wherein said providing includes selecting the estimate to generally maintain mass balance of the particles, and the estimate corresponds to an expected form of the size distribution of the particles.

24. The method of claim 22, wherein the calculated isotropic scattering coefficient is determined with an equation having an estimated product of the size distribution and the volume fraction as an argument.

25. The method of claim 19, wherein the particle interaction parameter is determined from a P-Y structure factor model.

26. A method of particle analysis, comprising:

(a) exposing a number of particles to a number of light wavelengths of predetermined time-varying intensity;

(b) detecting multiply scattered light from the particles in response to said exposing to determine a number of values each corresponding to a different one of the wavelengths, the values each being representative of a time-of-flight characteristic of the particles; and

(c) providing an output determined from the values, the output corresponding to at least one of a particle size distribution, particle volume fraction, or a particle interaction parameter, the particle interaction parameter

corresponding to at least one of a particle size distribution, particle volume fraction, or a particle interaction parameter, the particle interaction parameter corresponding to a nonlinear relationship between particle concentration and an isotropic scattering coefficient for the particles.

20. The method of claim 19, further comprising controlling a process in accordance with the output.

21. The method of claim 19, wherein said providing includes determining the observed isotropic scattering coefficient and an absorption coefficient for the particles for each of the wavelengths from a corresponding one of the values.

22. The method of claim 19, wherein said providing includes:

(i) determining an observed isotropic scattering coefficient for the particles for each of the wavelengths from a corresponding one of the values;

(ii) establishing an estimate corresponding to at least one of the size distribution or the volume fraction;

(iii) determining a calculated isotropic scattering coefficient for each of the wavelengths from the estimate;

(iv) comparing the observed and calculated isotropic scattering coefficients to establish an error;

(v) changing the estimate; and

(vi) repeating said calculating, comparing, and changing until the

responsive to said output to regulate a reaction involving the particles.

16. The system of claim 14, wherein said calculation means includes an estimating means for iteratively determining said size distribution or said volume fraction as a function of mass of the particles.

17. The system of claim 14, wherein said structure factor is dependent on said particle size distribution and said particle volume fraction, and corresponds to a P-Y hard sphere model.

18. The system of claim 14, wherein said calculation means includes a number of parameters corresponding to a Weibull distribution.

19. A method of particle analysis, comprising:

(a) exposing a medium with a number of suspended particles to a number of light wavelengths, the wavelengths each being intensity-modulated at a predetermined frequency;

(b) detecting multiply scattered light from the medium in response to said exposing to characterize propagation of the multiply scattered light through the medium with a number of values, the values each corresponding to a different one of the wavelengths and each being representative of at least one of a phase or an amplitude of the multiply scattered light relative to the predetermined frequency; and

(c) providing an output determined from the values, the output

14. A system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light, comprising:

(a) a light source with a predetermined time-varying intensity configured to expose the medium to a number of different wavelengths of light;

(b) a sensor spaced apart from said source, said sensor being configured to provide a detected light signal corresponding to multiply scattered light from the particles at the different wavelengths in response to exposure to said source;

(c) a processor responsive to said detected light signal, said processor including a calculation means for generating an output signal corresponding to at least one of particle size distribution, particle volume fraction, or a structure factor determined in accordance with an observed isotropic scattering coefficient of the medium, said structure factor being representative of particle interactions that influence light scattering behavior of said particles, said processor being configured to determine a value representative of said observed isotropic scattering coefficient from said detected light signal; and

(d) an output device responsive to said output signal to provide an output corresponding to said at least one of said particle size distribution, said particle volume fraction, or said structure factor of the particles.

15. The system of claim 14, further comprising a reaction vessel containing the particles and the medium, and wherein said output device includes a control element operatively coupled to said reaction vessel and

9. The system of claim 8, further comprising a reaction vessel containing the particles and medium, and wherein said output device includes a control element operatively coupled to said reaction vessel and responsive to said output to regulate a process involving the particles.

10. The system of claim 8, wherein said processor is further configured to determine said size distribution or volume fraction as a function of mass of the particles.

11. The system of claim 8, further comprising a second sensor providing a second detection signal, said comparison signals being determined as a function of said first and second detection signals for each of the wavelengths.

12. The system of claim 8, wherein said processor further determines a structure factor indicative of particle-to-particle interactions, said structure factor varying in accordance with concentration of the particles in the medium.

13. The system of claim 8, wherein said processor is configured to generate a particle interaction signal representative of particle-to-particle interactions that vary with particle concentration and influence light scattering behavior of the particles.

and a third value corresponding to mass of the particles.

8. A system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light comprising:

a light source with a predetermined time-varying intensity configured to expose the medium to a number of different predetermined wavelengths of incident light;

a first sensor spaced apart from said source, said first sensor being configured to provide a first detection signal corresponding to detected light, the detected light being multiply scattered by the particles;

a processor responsive to the first detection signal and being configured to receive an exposure signal corresponding to said incident light, said processor being configured to generate: (a) a number of comparison signals each corresponding to a difference with respect to time between the detected light and the incident light for a corresponding one of the wavelengths, (b) a number of scattering signals each correspondingly determined from the comparison signals and each corresponding to an observed isotropic scattering coefficient of the medium for a different one of the wavelengths, and (c) an output signal indicative of one of size distribution or volume fraction of the particles, said output signal being determined as a function of said scattering signals; and

an output device responsive to said output signal to provide an output corresponding to the size distribution or volume fraction of the particles.

as a function of the estimate and determining the estimate to generally maintain mass balance.

4. The method of claim 1, wherein the estimate corresponds to one of a number of parameters for an expected form of the size distribution.

5. The method of claim 4, wherein the incident light includes a number of different wavelengths of light, the first value is determined for each of the wavelengths, the parameters correspond to a Weibull distribution, and said calculating includes:

(i) establishing a number of particle size increments;

(ii) determining a scattering efficiency and a mean cosine of scattering angle as a function of the wavelengths and the increments; and

(iii) performing a first summation over a range of the particle sizes for each of the wavelengths, the first summation having the parameters, the scattering efficiency, and the mean cosine of scattering angle as arguments.

6. The method of claim 5, wherein said comparing includes performing a second summation over a range of the wavelengths, the second summation including a numerical difference between the first and second values as an argument.

7. The method of claim 5, wherein said changing includes updating the parameters as a function of the wavelengths, the first and second values,

CLAIMS

What is claimed is:

1. A method of particle analysis, comprising:

(a) exposing a number of particles in suspension to an incident light with a predetermined time-varying intensity, the particles being sufficiently close to one another to multiply scatter light;

(b) detecting multiply scattered light from the particles in response to the incident light to determine a first value corresponding to an observed isotropic scattering coefficient of the particles;

(c) establishing an estimate corresponding to at least one of volume fraction or size distribution of the particles;

(d) calculating a second value from the estimate, the second value corresponding to a calculated isotropic scattering coefficient;

(e) comparing the first and second values to establish an error;

(f) changing the estimate; and

(g) repeating said calculating, comparing, and changing until the error reaches a desired minimum.

2. The method of claim 1, wherein the incident light includes a number of different wavelengths of light, the first value is determined for each of the wavelengths, and said establishing, said calculating, said comparing, and said changing are performed for each of the different wavelengths.

3. The method of claim 1, further comprising controlling a process

embodiments have been shown and described and that all changes and modifications that come within the spirit of the invention are desired to be protected.

a fluid medium is determinable through measurements of multiplied scattered light in accordance with the present invention. Thus, the determination of liquid droplet size distribution to assess dispersion processes is a significant problem in industry that may be addressed by the present invention.

In another embodiment, particle analysis techniques of the present invention include monitoring processes involving genetically engineered microbes. For example, the production of insulin in the granules of genetically engineered E. coli bacteria may be monitored to provide rapid feedback for optimization of the insulin production process.

Also, it should be appreciated that the present invention finds application in many process involving the distribution of fine particles, including, but not limited to: processes involving a dispersion of liquid or solid particles in a fluid medium; chemical reactions having particles of mixed phases (such as solids and liquid droplets dispersed together in a common fluid medium); and the mechanical formation of particles.

All publications, patents and patent applications cited in this specification are herein incorporated by reference as if each individual publication, patent, or patent application were specifically and individually indicated to be incorporated by reference. Copending U.S Patent Application Nos. 08/747,112, filed 8 November 1996, and 60/050,809, filed 26 June 1997 are hereby incorporated by reference as if set-forth completely herein. While the invention has been illustrated and described in detail in the drawings and foregoing description, the same is to be considered as illustrative and not restrictive in character, it being understood that only the preferred

nanometers with the illustrated distributions being normalized to the peak value (vertical axis). Noise levels of 0%, 1%, and 5%, respectively, are shown in FIGS. 17a-17c. The results are tabulated in table 6 as follows:

	Actual Parameters	0% Noise	1% Noise	5% Noise
Mean Diameter (nm)	250	250	253.4	243.9
Percent Error (%)	----	0.00	1.36	2.44
Deviation (nm)	50	50	48.3	32.9
Percent Error (%)	----	0.00	3.4	34.2
Volume Fraction	0.31	0.31	0.314	0.291
Percent Error (%)	----	0.00	0.127	6.13
Δr (nm)	25	25	22.7	28.6
Percent Error (%)	----	0.00	9.2	14.4

Table 6: Summary of Recovered Distribution for Soft Sphere Model

This table indicates that the soft sphere model facilitates a good recovery of mean and volume fraction values despite the presence of noise.

Because the photon migration measurements of the present invention depend upon differences in refractive indices between the dispersed particles and the surrounding fluid, the size distribution of a liquid droplet dispersion in

straight, solid line corresponds to the linear relationship of isotropic scattering coefficients to particle concentration when particle interactions are ignored (the structure factor equal to unity, $S(q)=1$); the circular symbols denote experimental measurements; and the dashed line indicates the nonlinear change of isotropic scattering coefficient with percent solids predicted by the P-Y hard sphere model. Notably, the P-Y model agrees well with the experimental data points, both illustrating a nonlinear relationship at higher concentrations. FIG. 16a shows the change in isotropic scattering coefficient with percent solids of the particles by volume at a wavelength of about 780 nanometers for a polydisperse polystyrene suspension with a mean particle diameter of about 0.4 micron. FIG. 16b shows the isotropic scattering coefficient at about 670 nanometers for a polydisperse polystyrene suspension having a mean particle diameter of about 0.15 micron. FIG. 16c illustrates the isotropic scattering coefficient at about a 670 nanometer wavelength for a polydisperse polystyrene suspension having a mean particle diameter of about 0.2 micron. It should be appreciated that the relationship between the isotropic scattering coefficient and particle concentration is generally linear at low concentration levels, and becomes increasingly nonlinear as the concentration level increases.

In yet another example, FIGS. 17a-17c illustrate the results of simulations of the soft sphere model for the structure factor. For these experiments, the inverse algorithm was applied to simulated measurements in the presence of various levels of noise. The particle size axis (the horizontal axis shown) was provided over a range between 15 nanometers and 1500

in accordance with the present invention for samples S1 and S2 corresponding to FIGS, 12a and 12b, respectively. A log-normal Gaussian distribution was assumed for f(x) in both cases. The mean size and standard deviation for samples S1 and S2 are correspondingly presented in tables 4 and 5 as follows:

	FDPM	DLS	X-ray
Mean (μm)	0.310	0.314	0.318
Std. Deviation (μm)	0.118	0.112	0.115
Volume Fraction-	0.0047	0.0045 (By Evaporation)	------------

Table 4: Titanium Dioxide Suspension Sample S1 (See FIG. 12a)

	FDPM	DLS	X-ray
Mean (μm)	0.318	0.375	0.359
Std. Deviation (μm)	0.079	0.143	0.145
Volume Fraction	0.0044	0.0045 (By Evaporation)	------------

Table 5: Titanium Dioxide Suspension Sample S2 (See FIG. 12b)

FIGS. 16a-16c comparatively illustrate the structure factor in terms of isotropic scattering coefficient (vertical axis) versus percent solids of particles by volume (horizontal axis). For each of FIGS. 16a-16c, the generally

TiO_2 particles does not appear to appreciably detract from the relative accuracy of the PSD determination.

FIGS. 12a-12b comparatively illustrate size distribution determinations using Frequency Domain Photon Migration (FDPM) analysis (solid line) of the present invention, Dynamic Light Scattering (DLS) (short dashed line), and X-ray scattering (long dashed line) for each of two samples of titanium dioxide suspensions, designated S1 and S2, respectively. For the purpose of FDPM measurements, 1000 milliliters (ml) of each sample was placed in a 14.6 centimeter (cm) cylinder glass vessel with an inside diameter of 11.1 cm. Sinusoidally modulated light was deliver to, and collected from each sample via optical fibers of 1000 micrometers in diameter. Both the source and the detector optical fibers were placed parallel to the axis of the cylinder with their tips close to the center of the vessel. Phase shift and amplitude modulation was measured over a modulation frequency range of about 16 megahertz (MHz) to 240 MHz. Relative phase shifts were calculated corresponding to relative source-detector separations ranging form 0.1 cm to 0.5 cm. Samples were gently stirred between measurements to prevent any sedimentation. The solution of the diffusion equation (1) for the transport of photons in multiply scattering solution with infinite media boundary condition was applied to the data of relative phase shifts at different modulation frequencies. Upon applying Marquardt-Levenberg nonlinear regression analysis to this data, isotropic scattering coefficients (μ_s') were obtained at seventeen different wavelengths ranging from 400 nanometers (nm) to 900 nm. Particle size distribution, f(x), and volume fraction, ϕ, were determined from these values

from experimental measurements for three different suspensions with the additional constraint of mass balance. The weighting parameter used for obtaining these results was a constant of 0.1. It has been discovered that a weighting parameter in the range between 0.01 and 0.2 works well for these samples. Table 3 presents the results from the volume fraction calculations for the three different suspensions as follows:

	Values of ϕ from Photon Migration (%)	Values of ϕ from DLS (%)
PP722	0.98	0.95
PP755	1.61	1.53
PP788	0.67	0.63

Table 3 Solids volume fractions for suspensions PP722, PP755 and PP788 obtained with mass balance constraint.

FIG. 12 illustrates a Photon Migration (PM) measurement of multiply scattered light to experimentally determine PSD (solid line) for an aqueous TiO_2 suspension following a procedure similar to the polystyrene suspensions described above. For comparison, size distributions obtained from Dynamic Light Scattering (DLS) (dashed line) and determined from Transmission Electron Microscopy (TEM) (circle symbols) are shown. It should be noted that the size distributions obtained from photon migration measurements straddled those obtained from DLS and TEM. The non-spherical nature of

for each inverse solution required a few seconds on a SunSparc 10 Workstation using the data gathered by the IBM compatible system. The 486 based IBM compatible computer and SunSparc 10 Workstation collectively provide one example a processor suitable for use with the present invention; however, in other embodiments, a single piece of dedicated equipment, or other arrangement is envisioned as would occur to one skilled in the art.

FIGS. 6 through 8 show reconstructed particle size distributions from experimental measurements for the three different suspensions without the mass balance constraint. The solid lines (PM) denote the reconstructed values from the photon migration measurements of multiply scattered light while the dashed lines represent the size distribution obtained from DLS for comparison. Table 2 presents the volume fraction determination for the three different suspensions, as follows:

	Values of ϕ from Photon Migration (%)	Values of ϕ from DLS (%)
PP722	1.16	0.95
PP755	1.82	1.53
PP788	0.75	0.63

Table 2 Solids volume fractions for suspensions PP722, PP755 and PP788 obtained without mass balance constraint.

FIGS. 9 through 11 display the reconstructed particle size distributions

Figure 4 illustrates the typical measurements of relative phase-shift, θ_{rel}, on 0.96% by volume PP722 sample as a function of modulation frequency at a wavelength of 800 nm. Measurements were conducted with source-detector separations $|\mathbf{r}_s-\mathbf{r}_d|$ of 2.0, 1.5, and 1.0 cm. Consequently, relative phase-shift was reported at relative detector-detector separations $|\mathbf{r}_{d1}-\mathbf{r}_{d2}|$ of 1.0 and 0.5 cm. It is noteworthy that the two sets of phase-shift data recorded for each of the 0.5 cm separations were approximately the same, and the relative phase-shift for the 1.0 cm separation was about twice as large as the relative phase shift corresponding to the 0.5 cm separations. This dependence of phase shift on the relative separation of the source and detection sites is consistent with presence of the $|\mathbf{r}_{d1}-\mathbf{r}_{d2}|$ term in equation (7).

FIG. 5 graphically depicts experimental values (x symbols) for isotropic scattering coefficients obtained for the PP722 sample from measurements of multiply scattered light at 10 wavelengths between 360 and 800 nm. Expected values (solid line) predicted by Mie theory were calculated with equation (3) from experimental volume fraction and PSD. These measurements were conducted without the use of any external reflectance or calibration standard.

The f(x) and ϕ for each of the three polydisperse suspensions were determined assuming a Weibull distribution both with and without the mass conservation constraint. The initial estimates of the reconstruction parameters a,b,c,d were up to 100% greater than the output parameters. The particle size distributions, f(x), and volume fraction, ϕ, required 5 iterations until the function χ^2 reached a desired minimum value. Computational time

detected with the reference PMT. In order to obtain values of relative phase-shift, θ_{rel}, measurements were conducted as the detecting fiber optic was moved with micrometer precision to distances of 1.0, 1.5, and 2.0 cm away from the source fiber optic. At each source-detector separation, measurements were conducted at 10 modulation frequencies ranging from 24 to 240 MHz. Relative phase-shift between any two source-detector separations was determined by subtracting the phase-shift measured at the farthest separation from that measured as a closer separation. By fitting experimentally measured relative phase-shift at varying modulation frequencies to equation (7) using Levenberg-Maraquardt non-linear least square regression, parameter estimates of μ_a and μ_s' were obtained.

Three polydisperse samples of polystyrene microsphere suspensions were characterized using frequency domain measurements of multiply scattered light with this instrumentation. The three polystyrene samples were obtained from DOW Chemical Company of Midland, Michigan and designated PP722, PP755, and PP788 with mean particle diameters of 0.5763, 0.2954, and 0.1685 microns, respectively, as determined by independent DLS measurements (Microtrac Ultrafine Particle Analyzer, Honeywell, Leeds and Northrup, St. Petersburg, FL). The concentration of solids for PP722, PP755, and PP788 were 47.95%, 52.74%, and 46.03% solids by volume respectively as determined through evaporation measurements. The samples were diluted about 50 times with deionized ultrafiltered water to obtain samples of approximately 1% solids by volume. This concentration results in an opaque solution suitable to multiply scatter light.

outer diameter and 8 inch height. The tank was filled with a sample having particles suspended in a fluid medium.

The light which propagated from the source fiber within the multiple scattering medium was collected by another fiber held vertically in place in the tank. The detected light was then delivered to a sample sensor, also a PMT, via an optic fiber. Fourier analysis of the 4 MHz pulse train delivered to the sample and reference PMT's yielded a series of harmonic intensity-modulation frequencies at multiples of 4 MHz, which upon application of heterodyne detection techniques permitted isolation of the individual intensity-modulated frequencies. Heterodyning was performed by gain modulating the reference and sample PMTs at a harmonic of the laser repetition rate plus an offset cross-correlation frequency of 100 Hz. Gain modulation was accomplished using a commercial electronics package (ISS, Champaign, IL) and a -3 dBm RF signal from a frequency synthesizer (Marconi Instruments Signal Generator 2022A) amplified by a power amp (model 1403LA, ENI, Rochester, NY). The resulting 100 Hz electronic signal from the heterodyned PMTs provided the frequency domain phase-shift and amplitude modulation information. A conventional data acquisition module (ISS, Champaign, IL) was employed in a 486 IBM compatible personal computer to collect the measurement data.

By sweeping the RF signals at varying harmonics of the laser repetition rates, measurements of phase-shift $\theta(\omega)$ and amplitude demodulation $M(\omega)$ of a multiply scattered photon density wave propagating at varying modulation frequencies were detected with the sample PMT relative to the incident light

EXPERIMENTAL SECTION

The present invention will be further described with reference to the following specific examples. It will be understood that these examples are illustrative and not restrictive in nature.

Experimental measurements to determine PSD and volume fraction where conducted with a instrumentation configuration substantially similar to system 20. This instrumentation included a 10W argon ion laser (Beam-Lok 2060, Spectra Physics, CA) which pumped a picosecond pulsed Titanium:Sapphire laser (model 3950B Tsunami, Spectra Physics, Mountain View, CA). The Ti:Sapphire laser produced an optical pulse train of equally spaced light pulses of 2 psec FWHM at a repetition rate of 80 MHz. The output beam was sent to a pulse picker (model 3980, Spectra Physics) having an AOM crystal to produce a pulse repetition rate of 4 MHz at 2 ps FWHM and a SHG crystal to provide for light wave frequency doubling (wavelength halving). As a result, wavelengths from 720 to 900 nm, and from 360 to 450 nm were available for selection. The average power exiting the AOM crystal and the frequency-doubler (SHG crystal) was 50 mW and 10 mW, respectively. Depending upon the wavelength desired, the pulsed laser beam from the AOM or frequency doubler was sent to a glass slide beam splitter 28 that directed approximately 20% of the light to a reference sensor, photomultiplier tube (PMT) (Hamamatsu R928, Hamamatsu, Japan), via a 1000 μm optical fiber (HCP-M1000T-08, Spectran, Avon, CT). The remaining light was directed to the scattering sample by another optical fiber which was held stationary and vertical in a clear acrylic cylindrical tank having a 9 inch

radius that accounts for the degree of particle interactions. Moreover, besides structure factor, other particle interaction parameters may be selected and applied in accordance with the present invention to account for variation in light scattering properties with particle concentration due to particle-to-particle interactions. Such particle interaction parameters generally characterize nonlinearity between a scattering property of the particles, such as the isotropic scattering coefficient, and the particle concentration level.

art.

In one such alternative structure factor model, the hard sphere model is modified to account for electronic affects beyond the particle surface. This phenomenon is particularly substantial for lower concentrations of electrolytes, where particle interactions are still significant. FIG. 14 comparatively represents this modification as a soft sphere SS next to hard sphere HS. Soft sphere SS has a "soft" outer shell region corresponding to the interactive reach of the particle beyond its surface. This "soft" region is designated by the radial extension increment Δr and accounts for the electronic forces extending beyond the surface of the particles. The effective electrostatic charge EC2 is shown as a broken line at $r + \Delta r$. The sum $r + \Delta r$ is treated as the "equivalent" hard sphere radius for the P-Y model which is otherwise applied in the same way as described above. FIG. 15 depicts the relationship of the isotropic scattering coefficient to light wavelength for the soft sphere model (diamond-shaped data points), the hard sphere model (triangular-shaped data points), and the unity structure factor, $S(q) = 1$ (square-shaped data points).

Regardless of the structure factor model selected, any of the embodiments previously described and any such variations as would occur to those skilled in the art may be adapted to incorporate the structure factor technique. By way of nonlimiting example, the mass balance constraint described in connection with equations (22)-(30) or the Weibull distribution simplification described in connection with equations (15)-(20) may be included in a process to determine a structure factor or effective hard sphere

which isotropic scattering coefficients for each wavelength $\left(\mu_{s'}\right)_j^c$ are calculated through the summation approximation of equation (31) for all wavelengths using the estimates of f(x) and ϕ, and the corresponding calculated values of S(q), g, and q_{scat}. After stage 642, control flows to stage 644 to determine χ^2 as described in connection with stage 544 of process 500. The χ^2 of observed and calculated coefficients is then compared to an error threshold in conditional 646 to determine if the current estimates of f(x) and ϕ are suitable for output. If conditional 646 is satisfied, control flows to stage 650 to output f(x), ϕ, and S(q). If conditional 646 is not satisfied, control flows to stage 648.

In stage 648, the estimation of f(x) and ϕ is updated. This update also includes recalculation of g and q_{scat} based on the current S(q) value. Once updates are performed in 648, loop 640 closes back on stage 642 to provide updated calculations of the corresponding isotropic scattering coefficients. Loop 640 is iteratively executed until the χ^2 difference is minimized to an acceptable level. The particle size distribution f(x), the volume fraction ϕ, and structure factor S(q) may be output in stage 650. Aside from the improved accuracy of size distribution estimation and volume fraction at high particle concentrations, the structure factor S(q) is useful in ascertaining information about the behavior of colloidal suspensions and emulsions. For example, the structure factor alone is useful in monitoring colloidal suspensions and predicting shelf-life of emulsions with respect to phase separation. In other embodiments, different particle structure factor models may be employed other than the P-Y hard sphere model as would occur to those skilled in the

$$\frac{1}{S(q)} = 1 + \frac{24\varphi}{x^3}\left\{\begin{array}{l} A(\sin x - x\cos x) + B\left[\left(\frac{2}{x} - 1\right)x\cos x + 2\sin x - \frac{2}{x}\right] \\ + \frac{\varphi A}{2}\left[\frac{24}{x^3} + 4\left(1 - \frac{6}{x^2}\right)\sin x - \left(1 - \frac{12}{x^2} + \frac{24}{x^4}\right)x\cos x\right] \end{array}\right\};$$

(32)

where: σ is the diameter of the particle determined from f(x); $x=q\sigma$; $\varphi=(\pi ND\sigma^3/6)$; ND=number density of particles determined from σ and ϕ; $A=[(1+2\varphi)^2/(1-\varphi)^4]$; and $B=[-3\varphi(\varphi+2)^2/2(1-\varphi)^4]$. It should be noted that $S(q)$ is a function of f(x) and ϕ.

FIG. 13 is a flow chart of process 600 which may be used to determine f(x), ϕ, and $S(q)$. Process 600 may be performed using system 20, system 120, or such other system as would occur to one skilled in the art. Stages 510-520 of process 600 are the same as the like numbered stages of process 500 described in connection with FIG. 2. After stage 520, stage 630 of process 600 is encountered. In stage 630, f(x) and ϕ are estimated and $S(q)$ is calculated. Notably, the determination of $S(q)$ is dependent on f(x) and ϕ estimates for this embodiment. The $S(q)$ calculation utilizes the mean particle diameter for σ as determined from the f(x) estimate, and the number density ND as determined from the f(x) and volume fraction ϕ estimates. Also, g and q_{scat} are initially determined to fit the calculated $S(q)$ to the measured isotropic coefficient μ_s' and absorption coefficient μ_a in accordance with a summation approximation of equation (31) for each wavelength λ_j.

Next, loop 640 is entered. In loop 640, stage 642 is encountered in

$$\mu_s' = \int_0^\infty \frac{3}{2x}\left[\int_0^\pi 2\pi\, q_{scat}(n,\lambda,r,\theta)\pi r^2\left(1-g(n,\lambda,r)\right)S(q)\phi\left(1-g(n,\lambda,x)\right)\sin(\theta)d\theta\right]\phi f(x)dx$$

(31)

where: q = equals $[(4\pi n/\lambda_j)\sin(\theta/2))]$ and q_{scat} is the angular scattering efficiency. The structure factor $S(q)$ accounts for nonrandom particle structure within the fluid that typically varies with concentration of the particles in the medium. For example, the electrostatic charge on suspended particles generally influences spacing and organization of substantially concentrated particles in a fluid, which in turn influences light scattering. For low concentrations, these forces are usually negligible, so the particles may be treated as random scatterers with $S(q) = 1$. For a structure factor of unity ($S(q) = 1$), the calculation of isotropic scattering coefficients μ_s' at each wavelength of interest is the same in equations (3) and (31). For higher concentrations, $S(q)$ typically varies with the structure imparted by the particle interactions.

One approach to ascertaining an appropriate $S(q)$ is to treat particles as hard spheres of radius r as represented in FIG. 14 by particle hard sphere HS. For a hard sphere, the electrostatic charge resides on the surface, as represented in FIG. 14 by broken line EC1. For this approximation, the Percus-Yevick (P-Y) hard sphere model may be employed to predict $S(q)$ as follows:

boundary conditions. In other embodiments, the present invention may be readily adapted to different boundary conditions. For example, in one alternative embodiment, a processing chamber or passageway containing the scattering media may be interrogated by detecting multiply scattered light that is reflected or backscattered by the media through a "viewing window" arrangement instead of directly immersing fibers in the media. This arrangement results in a reflectance boundary condition. The present invention may be adapted using techniques known to those skilled in the art to accommodate this reflectance geometry or such other boundary conditions as may arise from a particular probe arrangement.

When the concentration of particles suspended in a medium is low (e.g. <2%), the particles act independently with regard to light scattering; however, as the concentration increases, interactions between suspended particles become more significant. These particle-to-particle interactions may impact accuracy of the $f(x)$ and ϕ determination in accordance with the present invention. Thus, a particle interaction parameter which accounts for concentration-dependent particle interactions that influence light scattering properties is desirable. Preferably, the determination of this particle interaction parameter may be incorporated into techniques of the present invention for determining $f(x)$ and ϕ.

For one preferred embodiment, a structure factor $S(q)$ for the particles has been found to be suitable as the particle interaction parameter. In this embodiment, the structure factor $S(q)$ is introduced by modifying the isotropic scattering coefficient (μ_s') determination of equation (3) as follows:

intensity. In other embodiments of the present invention, the light source arrangement is configured to provide wavelengths and time-varying intensity suitable for interrogation of the particular process being monitored using techniques known to those skilled in the art.

Analyzer 150 also includes optical fiber 134 to detect re-emitted light from the particles in vessel 160 after multiple scattering. It is preferred that analyzer 150 be of rugged design suitable for industrial applications. Analyzer 150 includes a processor configured to execute software to determine values representative of PSD or volume fraction in accordance with the present invention. Furthermore, analyzer 150 is also operatively coupled to control elements 170 which are used to regulate processing in vessel 160. By way of non-limiting example, elements 170 may include valves, heaters, or agitation devices electronically regulated by analyzer 150. Analyzer 150 is further configured with appropriate programming and interfaces to provide one or more output signals to control elements 170 as a function of PSD or volume fraction. Thus, system 120 provides a closed loop feedback control system capability for regulating chemical processes from on-line measurement of PSD and/or volume fraction.

Systems 20 and 120 of FIGS. 1 and 3, respectively, are described with corresponding light source fibers 30, 130 and detecting fibers 36, 136 geometrically arranged to approximate infinite boundary conditions -- such that light travelling from fibers 30, 130 to fibers 36, 136 does not encounter a substantial boundary. Equations (6) or (7) are applied to determine the isotropic scattering coefficient μ_s' and the absorption μ_a under such infinite

$$V_4 = w\left[M_t - \int_0^\infty \rho \frac{1}{12}\pi x^3 \phi f(x)dx\right]\int_0^\infty \rho \frac{1}{12} x^3 f(x)dx \qquad (30)$$

This mass balance constraint serves as an additional regularization scheme and typically provides further stabilization.

FIG. 3 depicts system 120 of an alternative embodiment of the present invention is depicted. System 120 includes analyzer 150 coupled to reaction vessel 160 by fibers 130 and 134. Analyzer 150 is configured to determine PSD and volume fraction for particles dispersed in a fluid medium in vessel 160 in accordance with the present invention. Generally, the optimum number and size of the wavelengths selected for interrogation depends on the nature of the particles, medium, and process involved. Furthermore, it has been discovered that typically fewer wavelengths may be required to determine volume fraction as compared to PSD for a given arrangement.

Analyzer 150 includes a light source configured to deliver light to vessel 160 via fiber 130. This light source may resemble source 21 of system 20, but preferably is a lamp-based or laser diode array system configured to provide light of a desired time-varying intensity at selected wavelengths. In one embodiment, system 120 includes an array of laser diodes which each correspond to a desired wavelength suitable for the particular process and material being interrogated in vessel 160. For this embodiment, the diodes are configured to provide incident (output) light with a sinusoidally modulated

$$\chi^2 = \sum_{j=\lambda_1}^{\lambda_M} [(\mu_s')_j^o - (\mu_s')_j^c]^2 + w\left[M_t - \int_0^\infty \rho \frac{1}{12} \pi x^3 \phi f(x) dx\right]^2 \tag{23}$$

where w is a weighting parameter. To efficiently update the estimate and account for the relationship of equation (23), the following Jacobian-based relationship is employed:

$$(\Im^T \Im + \Re + \alpha I)\Delta\varsigma = \Im^T[(\mu_s')^o - (\mu_s')^c] + V \tag{24}$$

where

$$\Re = \begin{bmatrix} \frac{\partial V_1}{\partial a} & \frac{\partial V_1}{\partial b} & \frac{\partial V_1}{\partial c} & \frac{\partial V_1}{\partial d} \\ \frac{\partial V_2}{\partial a} & \frac{\partial V_2}{\partial b} & \frac{\partial V_2}{\partial c} & \frac{\partial V_2}{\partial d} \\ \frac{\partial V_3}{\partial a} & \frac{\partial V_3}{\partial b} & \frac{\partial V_3}{\partial c} & \frac{\partial V_3}{\partial d} \\ \frac{\partial V_4}{\partial a} & \frac{\partial V_4}{\partial b} & \frac{\partial V_4}{\partial c} & \frac{\partial V_4}{\partial d} \end{bmatrix} \tag{25}$$

$$V = (V_1, V_2, V_3, V_4)^T \tag{26}$$

$$V_1 = w\left[M_t - \int_0^\infty \rho \frac{1}{12} \pi x^3 \phi f(x) dx\right] \int_0^\infty \rho \frac{1}{12} \pi x^3 \phi \frac{\partial f(x)}{\partial a} dx \tag{27}$$

$$V_2 = w\left[M_t - \int_0^\infty \rho \frac{1}{12} \pi x^3 \phi f(x) dx\right] \int_0^\infty \rho \frac{1}{12} \pi x^3 \phi \frac{\partial f(x)}{\partial b} dx \tag{28}$$

$$V_3 = w\left[M_t - \int_0^\infty \rho \frac{1}{12} \pi x^3 \phi f(x) dx\right] \int_0^\infty \rho \frac{1}{12} \pi x^3 \phi \frac{\partial f(x)}{\partial c} dx \tag{29}$$

particle sizes which surround the pth particle size. Current experiments have shown ξ=0.35 to be one preferred condition for the filter. This low pass filter typically enhances the particle size distribution recovery considerably by relaxing the requirement of the selected type of size distribution. It should be appreciated that the wider the distribution, the larger the required filter width for enhanced reconstruction. From the "filtered" f(x), the calculated isotropic scattering coefficient $(\mu_{s'})_j^c$ is computed for updating the Jacobian matrix.

In still a further embodiment, calculation of the inverse solution is improved when the total mass of the particles M_t and the mass density ρ are known. For this embodiment, the estimation of f(x) and ϕ focuses not only on the comparison of observed and calculated isotropic scattering coefficients, but also compares the known total particle mass to the mass obtained as a function of ρ and the estimates as follows:

$$M_t = \int_0^\infty \rho \frac{1}{12}\pi\, x^3[\phi f(x)]dx\,. \tag{22}$$

For some process configurations "mass balance" may often serve as a process control parameter in addition to PSD and volume fraction. For example, in emulsion polymerization processes, the total mass of monomer dispersed prior to initiation of polymerization is known. Proper reconstruction of the size distribution of the dispersed monomer phase should enable prediction of the total mass of dispersed monomer. Disappearance of the mass of monomer should reappear as mass of polymer. To include this mass balance constraint in the algorithm, we consider it as a constraint in the least squares minimization comparison as follows:

$$\Im = \begin{bmatrix} \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial a} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial b} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial c} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial d} \\ \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial a} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial b} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial c} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial d} \\ \frac{\partial(\mu_s^M)^c_{\lambda_M}}{\partial a} & \frac{\partial(\mu_s^M)^c_{\lambda_M}}{\partial b} & \frac{\partial(\mu_s^M)^c_{\lambda_M}}{\partial c} & \frac{\partial(\mu_s^M)^c_{\lambda_M}}{\partial d} \end{bmatrix} \tag{18}$$

The elements of the Jacobian are numerically computed using equation (3). The vectors, $(\mu_s')^o$ and $(\mu_s')^c$ contain the observed and computed values of isotropic scattering coefficients at the wavelengths of interest:

$$(\mu_s')^o = ((\mu_s')^o_{\lambda_1}, (\mu_s')^o_{\lambda_2}, \ldots (\mu_s')^o_{\lambda_M}), \qquad (\mu_s')^c = ((\mu_s')^c_{\lambda_1}, (\mu_s')^c_{\lambda_2}, \ldots (\mu_s')^c_{\lambda_M}) \tag{19}$$

$\Delta\zeta$ is the vector updating the four parameters, a, b, c and d:

$$\Delta\zeta = (\delta a, \delta b, \delta c, \delta d)^T \tag{20}$$

Thus, the particle sizing task now becomes to recover the four parameters (a, b, c and d) to describe f(x) and ϕ using the approach described in connection with loop 540.

In still another embodiment, a low pass filter is employed to smooth the estimate based on the parameters for an expected form of distribution, such as the Weibull distribution. In this embodiment, the size distribution is computed from the parameters and then subjected to a digital low pass filter by averaging over a window of $N^*\Delta x$.

$$f(x_p)^{new} = (1-\xi)f(x_p)^{old} + \frac{\xi}{N*}\sum_{l=p-\frac{N*}{2}}^{l=p+\frac{N*}{2}} f(x_l)^{old} \tag{21}$$

where ξ is a factor between 0 and 1, and the summation is over the N^*

assuming an expected form of the PSD. Generally, particulate processes can usually be characterized by Gaussian or log-normal distributions, both of which can be represented by proper parametric choices for a Weibull distribution described as follows:

$$f(x) = \frac{c}{b}\left[\frac{(x-a)}{b}\right]^{c-a} \exp\left[-\left(\frac{x-a}{b}\right)^{c}\right] \qquad (15)$$

where a, b and c describe the peak location, width, and shape, respectively, of the distribution. For this embodiment, d corresponds to ϕ, and the equation (3) summation approximation becomes:

$$(\mu_s')_j^c = \sum_{i=1}^{z} \frac{3}{2} \frac{Q_{scat}(\lambda_j, n, x_i)}{x_i}\left(1-g(\lambda_j, n, x_i)\right)\left\{d\frac{c}{b}\left(\frac{x_i-a}{b}\right)^{(c-a)} \exp\left[-\left(\frac{x_i-a}{b}\right)^{c}\right]\right\}\Delta x$$

(16)

where the expected range of particle diameter x from x_{min} to x_{max} is determined and incremented into k number of discrete sizes $x_i = x_{min} + (i-1)\,\Delta x$, $\Delta x = (x_{max} - x_{min}) / (z-1)$ for i=1 to z, and the terms $Q_{scat}(\lambda_j, n, x_i)$ and $g(\lambda_j, n, x_i)$ are determined from look-up tables based on λ_j, n, x_i.

Using Newton's method, the updates based estimation of the a,b,c,d parameters can be obtained from the resulting system of equations:

$$\Im^T \Im \Delta\zeta = \Im^T[(\mu_s')^o - (\mu_s')^c] \qquad (17)$$

where the Jacobian matrix $\Im$ now represents the sensitivity of isotropic scattering coefficients measured at wavelengths j=1,M upon the four parameters (a, b, c and d):

photon quantity in terms of intensity I(t), and the horizontal axis represents time t. The TOF distribution may be employed to obtain the observed isotropic scattering coefficient by applying the time domain form of the diffusion equation. Typically, time of flight values are in the range of picoseconds to a few nanoseconds.

In comparison, the measurement of intensity modulated light propagation in the frequency domain in accordance with equations (1)-(7) and accompanying text is provided in terms of phase shift θ and amplitude modulation M in FIG. 2b. Phase shift θ is represented by the left vertical axis, amplitude modulation M is represented by the right vertical axis, and frequency is represented by the horizontal axis which increases from left to right. The relationship of frequency to phase shift is characterized by the continuous curve that increases with increasing frequency (as designated by the left-pointing arrow) and the relationship of frequency to amplitude modulation is characterized by the continuous curve which decreases with increasing frequency (as designated by the right-pointing arrow).

It should be appreciated the "time-of-flight" characteristics of a scattering medium alternatively may be described in terms of phase shift and amplitude modulation relative to the modulation frequency. Notably, in both the frequency domain and time domain approaches, an intrinsic optical characteristic or optical property of the particles, such as isotropic scattering and absorption coefficients, may be determined from a time-based propagation measurement of multiply scattered light relative to input light.

In another embodiment, the determination of f(x) and ϕ is simplified by

Once the estimate is updated in stage 548, control returns to stage 542, via loop 540 to calculate the isotropic scattering coefficients based on the updated estimate. Repeated executions of loop 540 are anticipated before the desired minimum value of χ^2 is obtained.

Preferably, stages and conditionals corresponding to reference numbers 520 to 550 are performed through a software routine executed by processor 50, and processor 50 is of a type suitable to perform the extensive calculations of process 500 in an adequate amount of time. Notably, the phase shift may be determined from detection at a single location $\mathbf{r_d}$ using equation (6) or at multiple locations to determine the θ_{rel} as a function of $\mathbf{r_{d1}}$ and $\mathbf{r_{d2}}$ using equation (7). Furthermore, instead of phase shift, process 500 may be adapted to determine f(x) and ϕ based on amplitude M measurements in the frequency domain.

Referring back to FIG. 1, it should be appreciated that the length of scattering path SP is longer than the straight, direct pathway from fiber 30 to fiber 36. This pathlength increase due to the scattering media also results in a comparatively longer propagation time or "time of flight." Because photons typically travel along many different paths in a scattering media, the varying times of flight of the photons is usually amenable to description in a time of flight distribution. Thus, in one alternative embodiment, the diffusion equation may be utilized to compare incident light to resulting multiply scattered light in the time domain. For example, FIG. 2a illustrates the relationship between an input light pulse LP of a selected wavelength to a corresponding "time of flight" response, shown as distribution TOF; where the vertical axis represents

$$\Im^T \Im \Delta\zeta = \Im^T [(\mu_s')^o - (\mu_s')^c] \quad (11)$$

which results in a system of linear equations that may be solved using Newton's method to obtain the vector $\Delta\zeta$ containing the update values of $\phi f(x)$ across all bins, h=1, N as follows:

$$\Delta\zeta = (\delta(\phi f(x))_1, \delta(\phi f(x))_2, \ldots \delta(\phi f(x))_N)^T \quad (12)$$

The vectors, $(\mu_s')^o$ and $(\mu_s')^c$ contain the observed and computed values of isotropic scattering coefficients at the wavelengths of interest, j=1,M are:

$$(\mu_s')^o = ((\mu_s')^o_{\lambda_1}, (\mu_s')^o_{\lambda_2}, \ldots (\mu_s')^o_{\lambda_M}), \qquad (\mu_s')^c = ((\mu_s')^c_{\lambda_1}, (\mu_s')^c_{\lambda_2}, \ldots (\mu_s')^c_{\lambda_M}) \quad (13)$$

The matrix $\Im^T\Im$ in equation (11) is sometimes ill-conditioned and may be more readily solved through regularization of the decomposition of $\Im^T\Im$. One type of regularization scheme is the Maraquardt-type which may be stated as:

$$(\Im^T \Im + \alpha I)\Delta\zeta = \Im^T [(\mu_s')^o - (\mu_s')^c] \quad (14)$$

where I is the identity matrix and α may be a scalar or a diagonal matrix. By adding a contribution to the diagonal terms in equation (14), we make $\Im^T\Im$ more diagonally dominant which improves its invertability. The parameter α is usually determined by trial and error. Jiang, H., Paulsen, K., Osterberg, U., Pogue, B. and M. Patterson, Optical image reconstruction using frequency-domain data: simulations and experiments, J. Opt.Soc. Am. A 13, 253-266 (1996) is cited as a source of additional information concerning these calculations.

where it is desired to minimize χ^2 so that it is less than or equal to an established error amount. Conditional 546 tests whether this minimization has taken place. If the minimum has been reached, then control flows to stage 550 and the estimate is provided as the measured product $\phi f(x)$. Subsequently, f(x) and ϕ may be separated by performing a summation approximation of $\int_0^\infty \phi f(x)dx = \phi$.

However, if conditional 546 is not satisfied, then control flows to stage 548 to improve the estimate of $\phi f(x)$. One embodiment for rapidly converging to the desired minimum error is through application of a Jacobian matrix relationship. Specifically, the product $\phi f(x)$ is divided into N number of bins representing $\phi f(x)_h$, where h = 1 to N. In order to update $\phi f(x)_h$ in each bin, the Jacobian matrix which describes the sensitivity of the isotropic scattering coefficient to changes in $\phi f(x)_h$ in each bin h and at each wavelength λ_j is computed. This Jacobian matrix is given by:

$$\Im = \begin{bmatrix} \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial(\phi f(x))_1} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial(\phi f(x))_2} & \cdots & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial(\phi f(x))_N} \\ \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial(\phi f(x))_1} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial(\phi f(x))_2} & \cdots & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial(\phi f(x))_N} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\partial(\mu_s')^c_{\lambda_M}}{\partial(\phi f(x))_1} & \frac{\partial(\mu_s')^c_{\lambda_M}}{\partial(\phi f(x))_2} & \cdots & \frac{\partial(\mu_s')^c_{\lambda_M}}{\partial(\phi f(x))_N} \end{bmatrix} \tag{10}$$

and each element is computed through a summation approximation of equation (3) with $\phi f(x)_h$ and $\phi f(x)_h + \Delta\phi f(x)_h$. The updates, $\delta\phi f(x)_h$, resulting from the differences between measured and computed isotropic scattering coefficients, can then be obtained from:

Once $(\mu_{s'})_j^o$ has been obtained in stage 520, stage 530 is encountered. Stage 530 initiates an algorithm to inversely solve equation (3) for the integrands f(x) and ϕ given $(\mu_{s'})_j^o$. This inverse solution starts by estimating the product $\phi f(x)$ in stage 530. Once this product is known, f(x) and ϕ may be separated by the relation $\int_0^\infty \phi f(x)dx = \phi$.

Next, iteration loop 540 is entered at stage 542. In stage 542, the isotropic scattering coefficients for each of the wavelengths of interest are calculated from equation (3) using the estimate of $\phi f(x)$. For this calculation, equation (3) is approximated by the summation equation (8) as follows:

$$(\mu_{s'})_j^c = \sum_{i=1}^{z} \frac{3}{2} \frac{Q_{scat}(\lambda_j, n, x_i)}{x_i} \left(1 - g(\lambda_j, n, x_i)\right) \phi f(x) \Delta x_i. \qquad (8)$$

For equation (8), an expected range of particle diameter x from x_{min} to x_{max} is determined and incremented into k number of discrete sizes $x_i = x_{min} + (i-1)\Delta x$, where $\Delta x = (x_{max} - x_{min}) / (z-1)$ for i=1 to z; and the terms $Q_{scat}(\lambda_j, n, x_i)$ and $g(\lambda_j, n, x_i)$ are determined from look-up tables based on λ_j, n, x_i. The resulting set of calculated isotropic scattering coefficients, $(\mu_{s'})_j^c$ are then compared to the observed isotropic scattering coefficients, $(\mu_{s'})_j^o$ in stage 544. This comparison is performed in accordance with:

$$\chi^2 = \sum_{j=\lambda_1}^{\lambda_M} [(\mu'_s)_j^o - (\mu'_s)_j^c]^2 \qquad (9)$$

Equations (6) and (7) may be expressed in terms of the absorption coefficient μ_a and isotropic scattering coefficient $\mu_{s'}=(1-g)\mu_s$ through the substitution of equation (2) for $D(\lambda)$. Therefore, given $\theta(\mathbf{r_d})$ or $\theta_{rel} = |\theta(\mathbf{r_{d1}}) - \theta(\mathbf{r_{d2}})|$ from the execution of loop 510, equations (6) and (7) may be fit, respectively, for an observed absorption coefficient μ_a and isotropic scattering coefficient $\mu_{s'}$ by applying a Levenberg-Maraquardt non-linear least square regression of the type disclosed in Press et al., <u>Numerical Recipes: The Art of Scientific Computing</u> (Cambridge University Press 1992) to the data tabulated as a result of the execution of loop 510 for each of the wavelengths of interest. Preferably, processor 50 accumulates the frequency domain information in memory and is programmed to execute a Levenberg-Maraquardt non-linear least square regression algorithm to provide these optical coefficients. The resulting observed isotropic scattering coefficients for the wavelengths λ_j are represented as $(\mu_{s'})_j^o$. Preferably, $(\mu_{s'})_j^o$ is obtained by applying equation (7) to θ_{rel} measurements in stage 520.

Unlike conventional PSD measurement systems, these frequency domain measurements offer the ability to monitor absorption and scattering properties in multiply scattering systems without the need for spectral calibration of lamps or detectors to an external standard. Also, because the absorption and isotropic scattering coefficients do not appear as a product in equation (7), regression of phase-shift data provides an efficient means of determining optical characteristics from measurements of multiply scattered light.

position, **rd**:

$$\theta(\mathbf{r_d},\omega,\lambda) = \tan^{-1}\frac{\mathrm{Im}\,\Phi(\mathbf{r_d},\omega,\lambda)}{\mathrm{Re}\,\Phi(\mathbf{r_d},\omega,\lambda)} \quad (4)$$

and

$$M(\mathbf{r_d},\omega,\lambda) = \sqrt{[\mathrm{Im}\,\Phi(\mathbf{r_d},\omega,\lambda)]^2 + [\mathrm{Re}\,\Phi(\mathbf{r_d},\omega,\lambda)]^2} \quad (5)$$

The solution to equation (1) can be obtained for reflectance or transillumination measurements on semi-infinite random media as well as for finite geometry's in which the source and detector are separated by distance |**rs**-**rd**|. For simplicity, an infinite geometry is assumed which results in the following approximation:

$$\theta(\mathbf{r_d},\omega,\lambda) \approx -|\mathbf{r_s}-\mathbf{r_d}|\sqrt{\frac{3\mu_s'(\lambda)\{(\mu_a(\lambda)c_n)^2+\omega^2\}^{\frac{1}{2}}}{c_n}}\,\sin\left[\tan^{-1}\left\{\frac{\omega}{\mu_a(\lambda)c_n}\right\}\right] \quad (6)$$

Measurement of phase-shift usually includes a contribution due to the electronics and photodetection systems. Upon conducting a spatially resolved phase-shift measurement at two or more consecutive detector positions, **rd1**, **rd2**, instrument errors are accounted for. The relative phase, θ_{rel} can then be predicted from the following relationship:

$$\theta_{rel}(\lambda)=\left|\theta(r_{d1})-\theta(r_{d2})\right|=\left|r_{d1}-r_{d2}\right|\left(\frac{c_n^2\mu_a^2(\lambda)+\omega^2}{c_n^2D^2(\lambda)}\right)^{\frac{1}{4}}\sin\left[\frac{1}{2}\tan^{-1}\left(\frac{\omega}{c_n\mu_a(\lambda)}\right)\right]$$

(7)

coefficients, ε, and concentration, [C], for all light absorbing constituents present; and D(λ) is an "optical diffusion coefficient" which is given by:

$$D(\lambda) = \frac{1}{3[\mu_a(\lambda) + (1-g)\mu_s(\lambda)]} \quad (2)$$

The following are cited as additional sources of information concerning these relationships. A. Ishimaru, Wave Propagation and Scattering in Random Media, Academic Press, New York (1976); S. Chandrasekhar, Radiative Transfer, Oxford University Press, New York (1960); and R. C. Haskell, Svaasand, L.O., Tsay, T-T, Feng, T-C., McAdams, M.S., and B.J. Tromberg, Boundary Conditions for the Diffusion Equation in Radiative Transfer, J. Opt. Soc. Am. A 11, 2727-2741 (1994).

The term $(1-g)\mu_S = \mu_S'$ is the isotropic scattering coefficient which arises from multiple scattering and is dependent upon the particle size distribution, f(x) (where x is the diameter of the particles), and the total volume fraction, ϕ as follows:

$$(1-g)\mu_s(\lambda) = \mu_s'(\lambda) = \int_0^\infty \frac{3Q_{scat}(x,n,\lambda)[1-g(x,n,\lambda)]}{2x} \phi f(x)dx \quad (3)$$

where g is the mean cosine of the scattering angle from a single particle and Q_{scat} is the scattering efficiency. Both quantities are computed using classical Mie theory. See G. F. Bohren, and D.R. Hoffman, Absorption and Scattering of Light by Small Particles, John Wiley, New York (1983) for additional information concerning this computation.

The real and imaginary parts of $\Phi(\mathbf{r_s}-\mathbf{r_d},\omega)$ can be used to predict the measured phase-shift, θ, and amplitude modulation, M, measured at detector

collected for the given λ_j and stored by processor 50. In one embodiment, phase error inherent in the instrumentation of system 20 is reduced by collecting the multiply scattered light in two locations, $\mathbf{r_{d1}}$ and $\mathbf{r_{d2}}$, and determining $\theta_{rel} = |\theta(\mathbf{r_{d1}}) - \theta(\mathbf{r_{d2}})|$ as more fully described in conjunction with stage 520.

Next, conditional 516 is encountered. Conditional 516 tests whether frequency domain information for all wavelengths of interest have been collected. If not, the next wavelength λ_{j+1} is selected by appropriate adjustments to source 21 and control flows back to stage 512; closing loop 510. After frequency domain information for all desired wavelengths has been collected, then conditional 516 is satisfied and control flows to stage 520.

In stage 520, the isotropic scattering coefficient for each of the wavelengths λ_j is determined. This determination is based on the diffusion equation model of light propagation. Under conditions of multiple scattering, the time-dependent light propagation can be accurately modeled by a diffusion equation written here in the frequency domain:

$$-D(\lambda)\nabla^2\Phi(\mathbf{r},\omega) + \frac{i\omega}{c_n(\lambda)}\Phi(\mathbf{r},\omega) + \mu_a(\lambda)\Phi(\mathbf{r},\omega) = \delta(\mathbf{r} - \mathbf{r}_s)m \qquad (1)$$

where $\Phi(\mathbf{r}, \omega)$ is the fluence of photons at position $\mathbf{r}$ within a propagating "photon density wave" modulated at frequency, ω; c_n is the speed of light through the medium; m is the depth of sinusoidal modulation of the source located at position $\mathbf{r_s}$; $\mu_a(\lambda)$ is the wavelength dependent absorption coefficient that is equal to $\sum \varepsilon[C]$, the sum of the product of extinction

j	index to wavelengths λ.
M	maximum number of wavelengths λ.
p	discrete low pass filter index.

VECTOR AND MATRIX VARIABLES

I	identity matrix.
r	position vector.
$\mathbf{r_s}$	position vector of the source fiber 30, [cm].
$\mathbf{r_d}$	position vector of the detector fiber 36, [cm].
ζ	Matrix containing updates to size distribution and volume fraction.
ξ	Discrete filter parameter.
$\Im$	Jacobian matrix describing changes in isotropic scattering with size distribution and volume fraction.

TABLE 1 Description of Selected Variables

Referring to FIGS. 1 and 2, process 500 begins by entering loop 510 at stage 512. In stage 512, particles P in medium M are exposed to pulses of light of wavelength λ_j from source 21 via fiber 30; where "j" is the wavelength index form j=1, M. The location of the source light is designated by position vector $\mathbf{r_s}$. In stage 514, multiply scattered light resulting from the exposure in stage 512 is collected at detector location $\mathbf{r_d}$ corresponding to the position of fiber 36. Frequency domain quantities relating to $\theta(\mathbf{r_d})$ and $M(\mathbf{r_d})$ are

α	regularization parameter.
χ^2	minimization function.
ϕ	dispersed phase or solids volume fraction.
Φ	photon fluence, equal to the local concentration of photons times the speed of light [photons/cm^2 sec].
θ	phase-shift of amplitude modulated light relative to incident light, [degrees or radians].
θ_{rel}	relative phase-shift between two different detectors at different positions [degrees or radians].
λ	wavelength of light.
μ_s	scattering coefficient, [cm^{-1}].
μ_a	absorption coefficient, [cm^{-1}].
$\mu_s'=(1-g)\mu_s$	isotropic scattering coefficient [cm^{-1}].
σ	mean particle diameter.
ω	modulation frequency.

SUPERSCRIPT VARIABLES

o	observed.
c	computed.

SUBSCRIPT VARIABLES

h	index to Jacobian bins.
i	index to particle diameter.

GENERAL VARIABLES

a,b,c,d	parameters governing the size distribution and volume fraction for inverse solution.
k	wavelength number, $k=2\pi/\lambda$ [nm^{-1}]
c_n	speed of light through random medium, [cm/sec].
D	optical diffusion coefficient [cm].
f(x)	particle size distribution (volume distribution) [dimensionless].
g	mean cosine of angular scatter.
r	radius of particle, [microns].
x	diameter of particle, [microns].
m	depth of sinusoidal intensity modulated light.
M	amplitude modulation of re-emitted, multiply scattered light.
n	relative refractive index of particle.
N	number of Jacobian Matrix bins.
ND	number density of particles in suspension
N^*	number of particle sizes for discrete filter application.
q	positive integer frequency multiple.
q	q is an intermediate variable, $q = [(4\pi n/\lambda)(\sin(\theta/2))]$.
Q_{scat}	scattering efficiency of single scatterer.
q_{scat}	angular scattering efficiency.
$S(q)$	structure factor.
z	number of discrete particle size increments.

digitize the output of sensors 34, 38 for subsequent analysis by processor 50. Processor 50 may be an electronic circuit comprised of one or more components. Similarly, processor 50 may be comprised of digital circuitry, analog circuitry, or both. Also, processor 50 may be programmable, an integrated state machine, or a hybrid combination thereof. Preferably, processor 50 is comprised of one or more devices of the a digitally programmable variety.

Processor 50 is coupled to at least one input device 54 and at least one output device 56. Preferably, input device 54 is a keyboard or input control of a conventional variety, and output device 56 is a Cathode Ray Tube (CRT) based video display, printer, or other image display system known to those skilled in the art. System 20 is well-suited to conveniently deliver and detect light pulses at a selected rate and wavelength in a laboratory setting. In other embodiments, the configuration of system 20 may vary to provide and sense light at selected wavelengths and with a desired time-varying intensity using techniques known to those skilled in the art.

FIG. 2 is a flow chart depicting process 500 which is performed using system 20. Preferably, processor 50 is configured to execute a program that performs at least the more calculation intensive aspects of process 500. With regard to these calculations, selected variables employed in the description of process 500 are presented as follows in Table 1:

Where the source 21 pulse repetition rate is ω and q is a whole number multiplier, heterodyne subsystem 40 gain modulates sensors 34, 38 at a harmonic $q\omega$ plus a cross-correlation frequency offset, $\Delta\omega$, using conventional techniques. For one embodiment, an RF signal from frequency synthesizer 44 (Marconi Instruments Signal Generator, model 2022A) is phase-locked to the pulse frequency of source 21 via divider 42 and outputs the gain modulation frequency of $q\omega + \Delta\omega$ for amplification by power amp 46 (model 1403LA, ENI, Rochester, NY). The output of power amp 46 modulates the signals from sensors 34, 38 resulting in a signal of frequency $\Delta\omega$ from each sensor 34, 38. Comparative frequency domain information, including phase-shift (θ) and relative magnitude (M) (also called demodulation amplitude) for harmonic frequency $q\omega$ of the pulsed laser light delivered to sensors 34, 38 is obtained by comparing these outputs. By changing q, measurement of phase shift (θ) and relative magnitude (M) may be obtained as a function of modulation frequency. Furthermore, by varying the wavelength (λ) of the output from source 21, the phase shift (θ) and relative magnitude (M) may be obtained as a function of λ.

In one embodiment, the source 21 pulse repetition rate is 80 MHz which is divided by 8 by divider 42 and input to synthesizer 44 to provide the phase-locked loop. A 4 MHz pulse train is selected with picker 26 and the corresponding cross-correlation offset frequency is 100 Hz. Synthesizer 44 is preferably a Marconi Instruments signal generator, model 2022A, and amplifier 46 is a model 1403LA available from ENI, Rochester, NY. Preferably, interface 152 is a conventional data acquisition module suitable to

λ and 0.5λ outputs are separated by a prism to provide two outputs collectively represented as beam 27. The λ output is selected for wavelengths in the 720 to 900 nm range, and the 0.5λ output is selected for wavelengths in the 360 to 450 nm range.

Beam 27 from source 21 is directed to a glass slide beam splitter 28 which splits beam 27 to direct about 80% along optical fiber 30 and the remaining 20% along fiber 32 to reference sensor 34. Light directed along fiber 30 enters sample tank 60 to encounter particles P suspended in fluid medium M. Particles P are sufficiently concentrated in medium M to multiply scatter light pulses entering by fiber 30. This multiple scattering is diagrammatically represented by scattering path SP. Multiply scattered light is collected by fiber 36, and is then directed to sample sensor 38. Preferably, sensors 34, 38 are Photomultiplier Tubes (PMTs), (Hamamatsu R928, Hamamatsu, Japan) and fibers 30, 32, 36 are 1000 mm optical fibers (HCP-M1000T-08, Spectran, Avon, CT); however, in other embodiments other sensor types and couplings are envisioned as would occur to one skilled in the art.

Sensors 34, 38 are operatively coupled to heterodyne subsystem 40 and processor 50 via interface 52. It should be appreciated that the light pulse train incident on sensors 34 and 38 may be described in terms of a number of intensity modulated frequencies which are multiples of the pulse repetition rate via Fourier analysis. Heterodyne subsystem 40 and processor 50 provide frequency domain information about light collected from sensors 34, 38 in terms of one or more of the intensity modulation frequencies.

rod and excite titanium ions of the rod. In response, a monochromatic, unidirectional optical pulse train of light pulses is produced which is designated beam 25. Preferably, beam 25 has generally equally spaced light pulses of 2 picoseconds (psec) Full Width Half Maximum (FWHM) at a repetition rate of about 80 Megahertz (MHz). The output power of beam 25 is preferably maintained at about 20% of the input power of beam 23.

Beam 25 is directed to pulse picker 26. Picker 26 provides two functional capabilities: (1) to select an output pulse frequency less than or equal to the pulse repetition rate of pulses from input beam 25 and (2) to selectively halve the wavelength (λ) of the input beam. The frequency selection capability is provided by directing beam 25 to an Acousto-Optic Modulator (AOM) crystal. The AOM crystal controllably diffracts pulses from the impinging beam 25 at an angle relative to the main beam in accordance with a electromagnetic Radio Frequency (RF) input. The rate of diffracted or "picked" pulses may be selected to provide a number of different output repetition rates less than or equal to the input frequency.

Picker 26 also includes a Second Harmonic Generation (SHG) crystal to selectively produce output wavelengths at one half the input wavelength λ. Picker 26 is configured so that beam 25 passes through the SHG crystal after the AOM crystal. The SHG crystal emits a single photon for every two photons absorbed. The energy level of the emitted photon is approximately double the energy of each of the two absorbed photons. As a result, the wavelength corresponding to the emitted photon is about one half and the frequency is about doubled compared to each of the two input photons. The

DESCRIPTION OF PREFERRED EMBODIMENTS

For the purposes of promoting an understanding of the principles of the invention, reference will now be made to the embodiments illustrated in the drawings and specific language will be used to describe the same. It will nevertheless be understood that no limitation of the scope of the invention is thereby intended. Any alterations and further modifications in the described techniques, systems, and devices, and any further applications of the principles of the invention as described herein are contemplated as would normally occur to one skilled in the art to which the invention relates.

FIG. 1 depicts an analysis system 20 of one embodiment of the present invention. System 20 includes a light source 21 which includes Argon ion laser 22, Titanium:Sapphire laser 24, and pulse conditioner 26. Laser 22 generates a monochromatic output beam 23 using electrical discharges in a conventional manner. In one preferred embodiment, laser 22 is provided by a Beam-Lok model 2060 laser available from Spectra Physics, CA which is configured to deliver a beam with a diameter of less than 2 millimeters (mm) at a wavelength of 514.5 nanometers (nm). A constant output power of the Beam-Lok model 2060 laser is selected from a range of 0 and 10 watts (W) for this embodiment.

Beam 23 from laser 22 is configured to "pump" laser 24 using conventional techniques. In one embodiment, source 21 includes a Tsunami Ti:Sapphire laser, model 3950B, available from Spectra Physics, Mountain View, CA for laser 24 and the Beam-Lok model 2060 for laser 22. Beam 23 is directed into a cavity of laser 24 to impinge upon a titanium-doped sapphire

dispersion of TiO_2 particles.

FIGS. 12a-12b are graphs depicting size distributions for aqueous dispersions of TiO_2 particles supplied as suspension samples S1 and S2, respectively, which compare measurement of size distribution in accordance with the present invention to measurements by Dynamic Light Scattering (DLS) and X-ray scattering techniques.

FIG. 13 is a flow chart illustrating another process of the present invention capable of performance, for example, by the systems of FIGS. 1 and 3.

FIG. 14 is a comparative schematic illustration of selected aspects of particle-to-particle interaction structure factor models of the present invention.

FIG. 15 is a graph comparing selected structure factor models in terms of isotropic scattering coefficient and light wavelength.

FIGS. 16a-16c are graphs comparing the relationship of the isotropic scattering coefficient with the percent solids by volume from polydisperse polystyrene particles in suspension having a mean diameter of about 0.4 micron, 0.2 micron, and 0.15 micron, respectively.

FIGS. 17a-17c are graphs depicting simulation results using a soft sphere particle-to-particle interaction structure factor model with simulated noise levels of 0%, 1%, and 5%, respectively.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic view of an analysis system of one embodiment of the present invention.

FIG. 2 is a flow chart illustrating one process of the present invention performed by the system of FIG. 1.

FIG. 2a is a graph illustrating a time domain measurement of a photon time-of-flight distribution resulting from an incident light pulse in a scattering media.

FIG. 2b is a graph illustrating the frequency domain measurement of light propagation in a scattering media in terms of phase shift, θ, and amplitude, M.

FIG. 3 is a schematic view of a chemical process control system of another embodiment of the present invention.

FIG. 4 is a graph depicting the relationship between phase shift and modulation frequency for a dispersion of DOW PP722 particles.

FIG. 5 is a graph depicting the isotropic scattering coefficient for a dispersion of DOW PP722 particles as a function of wavelength.

FIGS. 6-8 are graphs depicting size distribution for DOW PP722, PP755, and PP788 particle dispersions without a mass balance constraint, respectively.

FIGS. 9-11 are graphs depicting size distribution for DOW PP722, PP755, and PP788 particle dispersions with a mass balance constraint, respectively.

FIGS. 12 is a graph depicting size distribution for an aqueous

algorithm to inversely solve for size distribution, volume fraction, or structure factor of a number of particles using observed values representative of the isotropic scattering coefficient of the particles at different wavelengths. This estimation may be based on an expected form of the distribution. Also, the estimation may account for mass of the particles.

An additional object of the present invention is to provide a technique for determining a particle interaction parameter which accounts for particle-to-particle interactions that vary with particle concentration and influence light scattering by the particles.

Further objects, advantages, features, forms, and aspects of the present invention will become apparent from the drawings and description contained herein.

provides a detected light signal corresponding to multiply scattered light from the particles at different wavelengths in response to exposure to the source. The processor is responsive to the emission signal and includes a calculation means for generating an output signal corresponding to at least one of a size distribution, volume fraction, or a structure factor of the particles in accordance with an observed isotropic scattering coefficient of the medium. The processor determines a value representative of the observed isotropic scattering coefficient from the detected light signal. The output device responds to the output signal to provide an output corresponding to at least one of the size distribution, the volume fraction, or the structure factor of the particles.

Accordingly, one object of the present invention is to determine particle size distribution, particle volume fraction, or a particle interaction parameter from multiply scattered light.

Another object of the present invention is to provide a self-calibrating system for the on-line determination of particle size distribution and volume fraction by detecting the propagation characteristics of multiply scattered light from particles dispersed in a fluid medium.

Yet another object is to determine one or more optical coefficients of a number of particles suspended in a medium by sensing propagation characteristics of multiply scattered light from the particles and to provide a size distribution or volume fraction of the particles from one or more optical coefficients.

Still another object of the present invention is to provide an estimation

expose the medium to a number of different predetermined wavelengths of incident light each having a predetermined time-varying intensity and a sensor spaced apart from the source. The sensor is configured to provide a detection signal corresponding to detected light. This detected light originates from the source and is multiply scattered by the particles. The system also includes a processor responsive to the first detection signal. The processor receives an exposure signal corresponding to the incident light and generates propagation signals by comparing the detection signal and the exposure signal for each of the wavelengths. These propagation signals characterize time of flight of the detected light through the medium resulting from multiple scattering by the particles. The processor is also configured to generate scattering signals corresponding to an isotropic scattering coefficient of the medium. The scattering signals are correspondingly determined from the propagation signals. The processor further generates an output signal indicative of one of size distribution or volume fraction of the particles which is determined from the scattering signals and a structure factor. This structure factor accounts for particle-to-particle interactions that influence light scattering behavior of the particles. The system further includes an output device responsive to the output signal to provide an output corresponding to the size distribution or volume fraction of the particles.

Yet another form of the present invention is a system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light. This system includes a light source, a sensor spaced apart from the light source, a processor, and an output device. The sensor

each other to multiply scatter light. Multiply scattered light is detected from the particles in response to the incident light to determine a first value corresponding to an observed isotropic scattering coefficient of the particles. An estimate corresponding to at least one of volume fraction or size distribution of the particles is established, and a second value is calculated as a function of the estimate. The second value corresponds to a calculated isotropic scattering coefficient. The first and second values are compared to establish an error, and the estimate is changed. The calculation of the second value, comparison of the first and second values, and changing of the estimate is repeated until the error reaches a desired minimum.

In still another form of the present invention, a method of analysis includes exposing a fluid with a number of suspended particles to an incident light. The particles are sufficiently concentrated in the fluid to scatter light. Multiply scattered light in response to this exposure is detected to determine a time-based value characteristic of propagation time of the multiply scattered light through the fluid. A quantity is determined as a function of the value which corresponds to an isotropic scattering coefficient of the fluid. An output is provided that corresponds to at least one of particle volume fraction, particle size distribution, or a particle interaction parameter corresponding to particle-to-particle interactions that influence light scattering behavior of the particles. The output is determined from the quantity.

A further form of the present invention is a system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light. This system includes a light source configured to

number of light wavelengths each being intensity-modulated at a predetermined frequency. Multiply scattered light from the medium in response to this exposure is detected to characterize propagation of the multiply scattered light through the medium with a number of values. The values each correspond to a different one of the wavelengths and are each representative of at least one of a phase or an amplitude of the multiply scattered light relative to the predetermined frequency. An output is provided that is determined from the values. The output corresponds to at least one of particle size distribution, volume fraction, or a particle interaction parameter. This particle interaction parameter corresponds to a nonlinear relationship between particle concentration and an isotropic scattering coefficient for the particles.

In an additional form, a number of particles suspended in a medium are exposed to a number of light wavelengths of predetermined time-varying intensity. Multiply scattered light form the particles in response to this exposure is detected to determine a number of values each corresponding to a different one of the wavelengths. These values are each representative of a time of flight characteristic of the particles. The output corresponds to at least one of particle size distribution, volume fraction, or a particle interaction parameter. This particle interaction parameter corresponds to a nonlinear relationship between particle concentration and an isotropic scattering coefficient for the particles.

In a further form, particles are exposed to an incident light with a predetermined time-varying intensity. The particles are sufficiently close to

More preferably, μ_s' is at least 100 times greater than μ_a. Also, as used herein "multiply scattered light" refers to light that has traveled at least 5 times the mean isotropic scattering length for a particular wavelength, defined as $1/\mu_s'$.

When light is multiply scattered by particles in a fluid, it typically travels a greater distance and therefore has a longer travel time as compared to a direct path through the fluid without encountering the particles. The "time of flight" of photons through a scattering media is on the order of about 1 nanosecond. Because many different scattering paths are likely, time of flight is usually characterized as a distribution; however, this distribution typically varies with the light wavelength, the refractive character of the particles relative to the media, the size of the particles, and the volume fraction of the particles. Thus, in a further form of the present invention, measurements corresponding to photon migration time or travel time through the scattering media may be obtained and utilized to characterize the particles.

At high particle concentrations, interactions between particles have a substantial influence on the light scattering properties of a multiple scattering media. This influence may degrade measurements which fail to account for particle-to-particle interactions. To adjust for particle interactions, a particle interaction parameter, which varies with particle concentration, may be utilized. In one form of the present invention, a particle structure factor is utilized, such as the Percus-Yevick model, which further provides an assessment of the stability of a corresponding particle suspension.

In another form, particles suspended in a medium are exposed to a

SUMMARY OF THE INVENTION

The invention relates to analysis of particles using photon migration techniques. Several aspects of the invention are novel, non-obvious, and provide various advantages. While the actual nature of the invention covered herein can only be determined with reference to the claims appended hereto, certain features which are characteristic of the present invention are described briefly as follows.

In one form of the present invention, particle size distribution or volume fraction of a number of particles in suspension is determined from the measurement of one or more propagation characteristics of multiply scattered light re-emitted from the suspension. As used herein, "particles" include crystals, solids, liquid droplets, microbes, or microbe organelles. Also, as used herein, "multiple scattering" of light refers to the condition where, at a given wavelength, a photon is more likely to be consecutively scattered many times between particles due to a refractive index mismatch between the dispersed particles and the host medium before being absorbed or detected. Generally, the multiple scattering condition entails that the particles be close enough to one another so that the distance a photon travels between scattering events is much smaller than the length traveled before absorption. Thus, multiple scattering of light occurs when $\mu_s' >> \mu_a$, where the absorption coefficient, μ_a, indicates the ability of a substance to absorb light of a particular wavelength, and the isotropic scattering coefficient, $(1-g)\mu_s=\mu_s'$, indicates the ability of a substance to scatter light of a particular wavelength in any particular direction. Preferably μ_s' is at least 10 times greater than μ_a.

various other system parameters. Also hampering the effectiveness of these techniques is the need to calibrate the equipment in situ. Process upsets, feedstock changes, or even normal batch process changes may invalidate the calibration. Depending upon the application, the sensor output for feedback control could be catastrophic absent proper calibration.

Thus, a need remains for a technique to analyze particles in a process stream which is self-calibrating and interrogates the process stream without requiring sampling or dilution. Preferably, this technique may be used to determine particle size distribution and volume fraction regardless of particle concentration level.

The focal position is made to vibrate at a high rate so that the beam travels significantly faster than particles in the medium. In theory, particles intercept the beam and reflect light for a duration of time which is proportional to the particle size. The reflected light is detected and timed, and a particle size is inferred from this information. To reconstruct a size distribution, the instrument counts the number of times each size occurs. Besides the constraint on speed of the beam relative to particle motion, tests have shown that this system consistently measures small particles as too large and large particles as too small. Also, the range swept by the laser beam must be smaller than the smallest particle size to be measured.

Similar to DLS and diffraction measurements, laser reflection techniques are based upon discrete single particle measurements to reconstruct PSD. Laser reflection measurements are sensitive to erroneous positioning of the focal plane, contribution of higher order scattering, and sampling error brought about by the hydrodynamic partitioning of large particles away from the wall and sensor head. In addition, the measurements are reported not to be accurate with non-opaque particles or dispersed droplets. Sparks, R.G., and C.L. Dobbs, The Use of Laser Backscatter Instrumentation for On-Line Measurement of the Particle Size Distribution of Emulsions, Part. Part. Syst. Charact. 10, 279-289 (1993) provides additional information concerning this technique.

Turbidity, DLS, Diffraction, and Laser reflection are all limited to some extent by the multiple scattering of light by the particles. These systems attempt to confine this problem by sampling and dilution, or by adjusting

statistical number of measurements can provide PSD's from diluted samples of particles.

Turbidity, DLS, and diffraction measurements all require careful calibration of the light source and detector to provide meaningful measurements. Also, the possibility that wavelength dependent sample absorbance will vary during normal process disturbances and feedstock changes threatens the accuracy of these techniques. More importantly, these approaches all require a relatively dilute sample compared to the usual process concentration in order to be effective.

Turbidity, DLS, and diffraction techniques suffer from other limitations which complicates on-line implementation. For example, on-line application of these techniques would require automated sampling procedures. For sizing solids, side stream measurements frequently create maintenance problems such as clogged pumps, conduits and filters within sampling devices. For sizing of liquid droplets, side stream measurements often induce coalescence and breakup. Furthermore the mechanical action of most automated sampling procedures may change the particle, crystal, or dispersed phase size distribution. Moreover, on-line measurements under these approaches may require substantial dilution, phase separation, or sample destruction to be effective.

One system which attempts to solve these problems is a laser reflection or "backscatter" technique, such as the PAR TEC 100 available from Laser Sensor Technology. This system includes a laser with a narrow beam focused directly into a polydisperse medium undergoing processing.

and F.R. Hallet, Spherical Particle Size Determination by Analytical Inversion of the UV-Visible-NIR Extinction Spectrum, Appl. Optics, 35, 193-200 (1996); and J. Vavra, Antalik, J., and M. Liska, Application of Regression Analysis in Spectroturbidity Size Characterization Methods, Part. Part. Syst. Charact. 12, 38-41 (1995) are cited as sources of additional information concerning turbidity based systems.

Another optical approach is Dynamic Light Scattering (DLS), also termed quasi-elastic light scattering or photon correlation spectroscopy. DLS systems monitor the fluctuation of light intensity due to the Brownian motion of a single particle into and out of the near-field. From the time-dependence of intensity fluctuations, the particle diffusion coefficient can be computed and the radius obtained from the Stokes-Einstein equation. A statistical number of measurements of diluted and pretreated samples can provide a PSD. Notably, DLS techniques are often used as the laboratory "standard" for spherical particles having a diameter of less than 10 microns. Thomas, J.C. and V. Dimonie, Fiber Optic Dynamic Light Scattering from Concentrated Dispersions. 3: Particle Sizing in Concentrates, Appl. Optics., 29, 5332-5335 (1990), and U.S. Patent Nos. 5,502,561 and 4,781,460 are cited as sources of additional background information concerning DLS techniques.

In still another approach, angular light scattering or "diffraction" measurements are employed which monitor the angular scatter of light at a single wavelength due to diffraction from a single particle. Using classical scattering theory and known refractive indices of fluid and particle, an equivalent radius can be computed from an inverse solution. Again, a

ability to determine PSD and the volume occupied by the dispersed particles (the "volume fraction") through "on-line" observation of the particles as they participate in the process remains elusive. These limitations adversely impact the development of optimal process controls for batch, semi-batch, and continuous reactors. The absence of this on-line measurement capability also impedes accurate model verification important in the formulation of a control model for non-linear processes. Typically, the lack of accurate modeling coupled with the lack of robust measurements have forced the use of open-loop control based upon less efficient downstream measurements; adversely impacting quality and efficiency.

Several laboratory particle sizing techniques exist, such as size-exclusion chromatography, capillary hydrodynamic fractionation, and photosedimentation; however, these techniques cannot provide on-line information about the process. Similarly, several optical techniques have been developed to provide PSD information. One of these techniques involves turbidity measurements which monitor the attenuation of light at multiple wavelengths traveling through a sample along a straight line path (180° relative to the incident light). Because these measurements do not account for backscatter nor multiple scattering of light back into the path length, turbidity analysis is only effective for diluted samples such that the product of turbidity, τ, and pathlength, L, is less than about 0.3. In other words, the optical path of the sample is no less than about three times the mean distance between scattering particles. Van de Hulst, H. Light Scattering by Small Particles Dover Publications, New York (1983); J. Wang,

or another designated dimension. For example, Particle Size Distribution (PSD) is highly relevant to the application, texture, and appearance of titanium dioxide based paint products. In addition, emulsion polymerization processes produce paints, various coatings, and synthetic rubbers to name only a few. Since emulsion polymerization involves the growth of suspended polymer particles, PSD measurements can yield insight into the extent of reaction and molecular weight distribution and can also provide means for product characterization. These measurements can also be adapted to many crystallization processes, such as in the food industry, pharmaceutics, agricultural products, and bulk chemicals. One way to optimize many of the processes involving a dispersion of particles is by providing on-line measurement of particle size distribution in combination with robust process control responsive to these measurements. Rawlings, J.B., Miller, S.M., and W.R. Witkowski, Model Identification and Control of Solution Crystallization Processes, Ind. Eng. Chem. Res., 32, 1275-1296 (1993); Farrell, R.J. and Y-C. Tsai, Nonlinear Controller for Batch Crystallization: Development and Experimental Demonstration, AIChE J., 41, 2318-2321 (1995); and Dimitratos, J., Elicabe, G., and C. Georgakis, Control of Emulsion Polymerization Reactors, AIChE J., 40, 1993-2021 (1994) are cited as additional sources of background information concerning chemical process control.

Despite the usefulness of PSD information, technology has not advanced such that these measurements can be made consistently under a wide variety of conditions and in a cost-effective manner. Moreover, the

PARTICLE ANALYSIS SYSTEM AND METHOD

CROSS-REFERENCES

This application is a continuation-in-part of U.S Patent Application No. 08/747,112, filed 8 November 1996 and claims the benefit of U.S. Provisional Application No. 60/050,809, filed 26 June 1997.

GOVERNMENT RIGHTS IN THE INVENTION

The U.S. Government has a paid-up license in this invention and the right in limited circumstances to require the patent owner to license others on reasonable terms as provided by the terms of the National Science Foundation Young Investigator Award No. BES-9496239 and the National Institutes of Health Research Center Development Award K04-CA68374.

BACKGROUND OF THE INVENTION

The present invention relates to the analysis of particles with multiply scattered light, and more particularly, but not exclusively, relates to the determination of size distribution and volume fraction of particles using photon migration techniques.

Today's chemical industry heavily relies on particulate or dispersed phase processes. The quality of many industrial products produced by these processes relates to the size distribution of the particles in terms of diameter

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/20539

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :G01N 21/51
US CL : 356/336
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 356/336, 335, 342

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	School of Chemical Engineering, Purdue University (West Lafayette, IN, USA), PAITHANKAR, D., "Particle size distribution estimation via solution of the inverse problem of multi-wavelength scattering coefficient measurements," August 1995.	14-15, 26-29, 32-33

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search: 04 MARCH 1998

Date of mailing of the international search report: 13/03/1998

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703) 305-3230

Authorized officer
RICHARD ROSENBERGER
Telephone No. (703) 308-0956

CONFIRMATION COPY OF PRIOR FACSIMILE

IN THE INTERNATIONAL BUREAU OF WIPO

In re PCT application of PURDUE RESEARCH FOUNDATION	Authorized Officer: Richard Rosenberger
International Application Number PCT/US97/20539	Mailing Date 12 May 1998
International Filing Date 07 November 1997	Agent's File Reference: PUR-63/75P
Title of Invention PARTICLE ANALYSIS SYSTEM AND METHOD	

RESPONSE TO THE INTERNATIONAL SEARCH REPORT

The International Bureau
WIPO
34, chemin des Colombettes
1211 Geneva 20
Switzerland

Dear Sir/Madam:

In response to the International Search Report mailed 13 March 1998, regarding the above-referenced PCT patent Application, applicant does not wish to make any amendments at this time.

Respectfully submitted

By L. Scott Paynter

L. Scott Paynter, #39,797
Woodard, Emhardt, Naughton,
Moriarty & McNett
Bank One Center/Tower, Suite 3700
111 Monument Circle
Indianapolis, Indiana 46204 US
(317) 634-3456

11164

CORRECTED VERSION*

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 **:** G01N 21/51	A1	**(11) International Publication Number:** **WO 98/20323** **(43) International Publication Date:** 14 May 1998 (14.05.98)

(21) International Application Number: PCT/US97/20539

(22) International Filing Date: 7 November 1997 (07.11.97)

(30) Priority Data:

08/747,112	8 November 1996 (08.11.96)	US
60/050,809	26 June 1997 (26.06.97)	US

(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications

US	08/747,112 (CIP)
Filed on	8 November 1996 (08.11.96)
US	60/050,809 (CIP)
Filed on	26 June 1997 (26.06.97)

(71) Applicant *(for all designated States except US)*: PURDUE RESEARCH FOUNDATION [US/US]; Office of Technology Transfer, 1650 Engineering Administration Building, Room 328 ENAD, West Lafayette, IN 47906 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: SEVICK-MURACA, Eva [US/US]; 7650 E. 100 N., Lafayette, IN 47905 (US). PIERCE, Joseph [US/US]; 309 Juniper Street, Lake Jackson, TX 77566 (US). RICHTER, Steven [US/US]; 16 Queens Court, Brunswick, GA 31521 (US). SHINDE, Rajesh [IN/US]; 1901 Union Street #126, Lafayette, IN 47904 (US). BALGI, Ganesh [IN/US]; 246 Longley Drive, Lebanon, IN 46052 (US). KAO, Jeffrey [US/US]; 301 Huckleberry Drive, Lake Jackson, TX 77566 (US). JIANG, Huabei [CN/US]; 205–05 Airport Road, West Lafayette, IN 47906 (US).

(74) Agents: PAYNTER, L., Scott et al.; Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, IN 46204 (US).

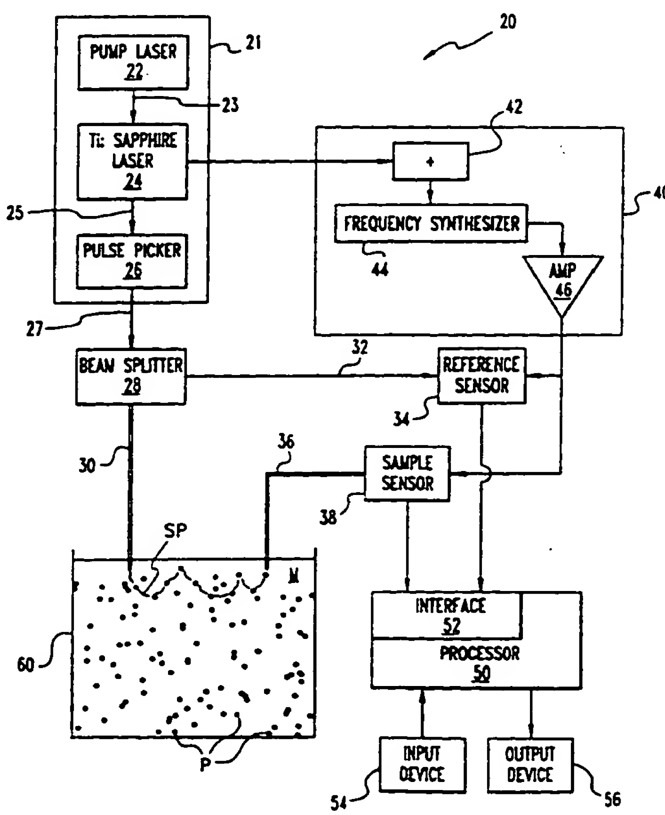
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: PARTICLE ANALYSIS SYSTEM AND METHOD

(57) Abstract

A system (20) and method are disclosed for the self-calibrating, on-line determination of size distribution f(x) and volume fraction ϕ of a number of particles (P) dispersed in a medium (M) by detecting one or more propagation characteristics of multiply scattered light from the particles (P). The multiply scattered light is re-emitted in response to exposure to a light source (21) configured to provide light at selected wavelengths. The determination includes calculating the isotropic scattering and absorption coefficients for the particles (P) by comparing the incident and detected light to determine a measurement corresponding to the propagation time through the scattering medium (M), and iteratively estimating the size distribution f(x) and volume fraction ϕ as a function of the coefficients for each of the wavelengths. An estimation approach based on an expected form of the distribution and the mass of the particles is also disclosed. Furthermore, techniques to determine a particle structure factor indicative of particle-to-particle interactions which vary with particle concentration and influence light scattering at high concentrations is disclosed.



*(Referred to in PCT Gazette No. 38/1998, Section II)

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US97/20539

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :G01N 21/51
US CL : 356/336
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 356/336, 335, 342

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	School of Chemical Engineering, Purdue University (West Lafayette, IN, USA), PAITHANKAR, D., "Particle size distribution estimation via solution of the inverse problem of multi-wavelength scattering coefficient measurements," August 1995.	14-15, 26-29, 32-33

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date		
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
04 MARCH 1998	13/03/1998

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	RICHARD ROSENBERGER
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0956

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PCT INTERNATIONAL APPL[...]TION TRANSMITTAL LETTER — DATE: 7 November 1997

REGARDING THE INTERNATIONAL A[...]ATI[redacted]OF — [redacted]T OR REFERENCE NUMBER

PURDUE RESEARCH FOUND[redacted]N , et al. — [redacted]-63/75P

ENTITLED

PARTICLE ANALYSIS SYSTEM AND METHOD

Certification under 37 CFR 1.10 (if applicable)

EM566457951US — 7 November 1997

"Express Mail" mailing number — Date of Deposit

I hereby certify that this application is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Linda C. Shelby — Linda C. Shelby

(Typed or printed name of person mailing application) — (Signature of person mailing application)

To the United States Receiving Office (RO/US):

Accompanying this transmittal letter is the above-identified International application, including a completed Request form (PCT/RO/101). Please process the application according to the provisions of the Patent Cooperation Treaty.

The following requests are made of the RO/US:

1. [X] PREPARATION AND TRANSMITTAL OF CERTIFIED COPY OF PRIORITY DOCUMENTS—Please prepare and transmit to the International Bureau a certified copy of the United States origin priority documents identified in Box VI of the Request form (37 CFR 1.451).

   To cover the cost of copy preparation and certification (37 CFR 1.19(a)(3) and (b)(1)),

   [X] a (check) (money order) in the amount of $ 30.00 included in fee ~~is attached~~ to this transmittal letter.

   [ ] the RO/US is hereby authorized to charge the following deposit account no.: ______.

2. [X] CHOICE OF INTERNATIONAL SEARCHING AUTHORITY—It is requested that the International Search be performed by the following International Searching Authority:

   [X] United States Patent and Trademark Office (ISA/US)

   [ ] European Patent Office (ISA/EP)

   The appropriate Search fee for the above-named Authority is indicated on the Fee Calculation Sheet (PCT/RO/101 Annex).

3. [X] SUPPLEMENTAL SEARCH FEES (ONLY WHEN ISA/US CONDUCTS THE INTERNATIONAL SEARCH.)—Please charge any Supplemental Search fees that may be required by the United States International Searching Authority (ISA/US) to deposit account no.: 23-3030.

   I understand that this authorization is subject to my oral confirmation thereof in each instance and that it in no way limits my right to submit a protest against payment of the Supplemental Search fees, but is merely an administrative aid to assure that the ISA/US may timely complete the Search Report.

NOTE: SUPPLEMENTAL SEARCH FEES FOR ISA/EP ARE PAYABLE DIRECTLY TO THE EUROPEAN PATENT OFFICE

4. [X] DISCLOSURE INFORMATION—In order to assist in screening the accompanying International application for purposes of determining whether a license for foreign transmittal should and could be granted and for other purposes, the following information is supplied:

   A. [ ] There is no prior filed application relating to this invention.

   B. [X] There is a prior application, serial number 08/747,112 filed on 08 November 1996 (08.11.96) and 60/050,809 ~~26 June 1997~~ (26.06.97) which contains subject matter that is

      1. [ ] substantially identical to that of the accompanying International application.

      2. [X] less than that of the accompanying International application. The additional subject matter of the International application appears on pages(s) and line(s) throughout the application.

      3. [ ] more than that of the accompanying International application.

   C. [ ] Disclosure information cannot be covered by the language of Points 4A or 4B above due to the involvement of several prior applications or for other reasons. A separate sheet on which the disclosure information is explained is attached to this transmittal letter.

5. [X] REQUEST FOR FOREIGN TRANSMITTAL LICENSE—According to the provisions of 35 U.S.C. 184 and 37 CFR 5.11, a license to transmit the accompanying International application to foreign agencies or international authorities is hereby requested.

SIGNER IS THE:

[ ] APPLICANT

[ ] COMMON REPRESENTATIVE

[X] (ATTORNEY) (AGENT)

REG NO 39,797

NAME OF SIGNER (typed): L. Scott PAYNTER

SIGNATURE: L Scott Paynter

PTO-1382 (REV 3-84)
USCOMM-DC 84 3817

U.S. Department of Commerce
Patent and Trademark Office

This sheet is not p[illegible] of and does not count as a sheet of the interna[illegible]nal application.

PCT

FEE CALCULATION SHEET
Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's file reference PUR-63/75P

Applicant
PURDUE RESEARCH FOUNDATION, et al.

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . 240 T
2. SEARCH FEE . . . . 450 S

International search to be carried out by US

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains 102 sheets.

first 30 sheets . . . . 530 b_1

72 x 10 = 720 b_2

remaining sheets additional amount

Add amounts entered at b_1 and b_2 and enter total at B . . . . 1250 B

Designation Fees

The international application contains 73 designations.

73 x 128 = 1408 D

number of designation fees payable *(maximum 11)* amount of designation fee

Add amounts entered at B and D and enter total at I . . . . 2658 I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT . . . . 30 P

5. TOTAL FEES PAYABLE

Add amounts entered at T, S, I and P, and enter total in the TOTAL box . . $3,378.00 TOTAL

☐ The designation fees are not paid at this time.

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- [X] is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.
- [ ] is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

23-3030
Deposit Account Number

7 November 1997
Date *(day/month/year)*

L Scott Paynter
Signature L. Scott PAYNTER 39,797

Form PCT/RO/101 (Annex) (January 1996; reprint July 1997)

See Notes to the fee calculation sheet

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only
International Application No.
International Filing Date
Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* PUR-63775P

Box No. I TITLE OF INVENTION

PARTICLE ANALYSIS SYSTEM AND METHOD

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

PURDUE RESEARCH FOUNDATION
Office of Technology Transfer
1650 Engineering Administration Building
Room 328 ENAD
West Lafayette, Indiana 47906
United States of America

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State *(i.e. country)* of nationality: US

State *(i.e. country)* of residence: US

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

SEVICK-MURACA, Eva
7650 E. 100 N.
Lafayette, Indiana 47905
United States of America

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: US

State *(i.e. country)* of residence: US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

PAYNTER, L. Scott
WOODARD, EMHARDT, NAUGHTON, MORIARTY & MCNETT
Bank One Center/Tower, Suite 3700
111 Monument Circle
Indianapolis, Indiana 46204 US

SEE CONTINUATION TO BOX NO. IV ON SHEET NO. 5

Telephone No. 317-634-3456

Facsimile No. 317-637-7561

Teleprinter No. 810-341-3283

☐ Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

PIERCE, Joseph
309 Juniper Street
Lake Jackson, Texas 77566
United States of America

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: US
State *(i.e. country)* of residence: US

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

RICHTER, Steven
16 Queens Court
Brunswick, Georgia 31521
United States of America

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: US
State *(i.e. country)* of residence: US

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

SHINDE, Rajesh
1901 Union Street #126
Lafayette, Indiana 47904
United States of America

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: IN
State *(i.e. country)* of residence: US

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

BALGI, Ganesh
246 Longley Drive
Lebanon, Indiana 46052
United States of America

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: IN
State *(i.e. country)* of residence: US

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

- [X] Further applicants and/or (further) inventors are indicated on another continuation sheet.

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

KAO, Jeffery
301 Huckleberry Drive
Lake Jackson, Texas 77566
United States of America

This person is:
- [ ] applicant only
- [x] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: US

State *(i.e. country)* of residence: US

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [x] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

JIANG, Huabei
205-05 Airport Road
West Lafayette, Indiana 47906
United States of America

This person is:
- [ ] applicant only
- [x] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: CN

State *(i.e. country)* of residence: US

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [x] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

This person is:
- [ ] applicant only
- [ ] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality:

State *(i.e. country)* of residence:

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [ ] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

This person is:
- [ ] applicant only
- [ ] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality:

State *(i.e. country)* of residence:

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [ ] the United States of America only
- [ ] the States indicated in the Supplemental Box

- [ ] Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*:

Regional Patent

- ☒ **AP ARIPO Patent:** GH Ghana, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* ....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

- ☒ AL Albania
- ☒ AM Armenia
- ☒ AT Austria
- ☒ AU Australia
- ☒ AZ Azerbaijan
- ☒ BA Bosnia and Herzegovina
- ☒ BB Barbados
- ☒ BG Bulgaria
- ☒ BR Brazil
- ☒ BY Belarus
- ☒ CA Canada
- ☒ CH and LI Switzerland and Liechtenstein
- ☒ CN China
- ☒ CU Cuba
- ☒ CZ Czech Republic
- ☒ DE Germany
- ☒ DK Denmark
- ☒ EE Estonia
- ☒ ES Spain
- ☒ FI Finland
- ☒ GB United Kingdom
- ☒ GE Georgia
- ☒ GH Ghana
- ☒ HU Hungary
- ☒ IL Israel
- ☒ IS Iceland
- ☒ JP Japan
- ☒ KE Kenya
- ☒ KG Kyrgyzstan
- ☒ KP Democratic People's Republic of Korea
- ☒ KR Republic of Korea
- ☒ KZ Kazakstan
- ☒ LC Saint Lucia
- ☒ LK Sri Lanka
- ☒ LR Liberia
- ☒ LS Lesotho
- ☒ LT Lithuania
- ☒ LU Luxembourg
- ☒ LV Latvia
- ☒ MD Republic of Moldova
- ☒ MG Madagascar
- ☒ MK The former Yugoslav Republic of Macedonia
- ☒ MN Mongolia
- ☒ MW Malawi
- ☒ MX Mexico
- ☒ NO Norway
- ☒ NZ New Zealand
- ☒ PL Poland
- ☒ PT Portugal
- ☒ RO Romania
- ☒ RU Russian Federation
- ☒ SD Sudan
- ☒ SE Sweden
- ☒ SG Singapore
- ☒ SI Slovenia
- ☒ SK Slovakia
- ☒ SL Sierra Leone
- ☒ TJ Tajikistan
- ☒ TM Turkmenistan
- ☒ TR Turkey
- ☒ TT Trinidad and Tobago
- ☒ UA Ukraine
- ☒ UG Uganda
- ☒ US United States of America ..... Continuation-in-Part
- ☒ UZ Uzbekistan
- ☒ VN Viet Nam
- ☒ YU Yugoslavia
- ☒ ZW Zimbabwe

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

- ☒ ID Indonesia
- ☐ ....
- ☐ ....
- ☐ ....
- ☐ ....

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of ______________.
The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)*

Supplemental Box *If the Supplem[illegible] Box is not used, this sheet need not be includ[illegible]he request.*

Use this box in the following cases:

1. If, in any of the Boxes, the space is insufficient to furnish all the information:

in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient;

in particular:

(i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available:

in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below;

(ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked:

in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;

(iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America:

in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;

(iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents:

in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;

(v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "Continuation" or "Continuation-in-part":

in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;

(vi) if there are more than three earlier applications whose priority is claimed:

in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI.

2. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty:

in such case, write "Statement Concerning Non-Prejudicial Disclosures or Exceptions to Lack of Novelty" and furnish that statement below.

Continuation to Box No. IV Agent

WOODARD, Harold R.; EMHARDT, C. David; NAUGHTON, Joseph A., Jr.; MORIARTY, John V.; McNETT, John C.; HENRY, Thomas Q.; DURLACHER, James M.; REEVES, Charles R.; WAGNER, Vincent O.; ZLATOS, Steve; BEREVESKOS, Spiro; BAHRET, William F.; BROWNING, Clifford W.; FRISK, R. Randall; LUEDERS, Daniel J.; BECK, Michael D.; GANDY, Kenneth A.; THOMAS, Timothy N.; SISSELMAN, Kerry P.; JONES, Kurt N.; ALLIE, John H.; MICHAEL, Jeffrey A.; BANTA, Holiday W.; COLE, Troy J.; PAYNTER, L. Scott; LOWES, J. Andrew; HARRIS, Darrin Wesley; SCHANTZ, Matthew R.; COY, Gregory B.; HIDAY, Lisa A.; DANILUCK, John V. and ROWE, James L., all of Woodard, Emhardt, Naughton, Moriarty & McNett, Bank One Center/Tower, Suite 3700, 111 Monument Circle, Indianapolis, Indiana 46204 United States of America

Continuation to Box No. V, DESIGNATION OF STATES
United States Patent Application
Serial No. 08/747,112 filed 8 November 1996 and
Serial No. 60/050,809 filed 26 June 1997

Sheet No. 6   Agent's Ref: PUR-63 /75P

Box No. VI PRIORITY CLAIM   Further priority claims are indicated in the Supplemental Box ☐

The priority of the following earlier application(s) is hereby claimed:

Country *(in which, or for which, the application was filed)*	Filing Date *(day/month/year)*	Application No.	Office of filing *(only for regional or international application)*
item (1) US	08 November 1996 (08.11.96)	08/747,112	
item (2) US	26 June 1997 (26.06.97)	60/050,809 (per postcard)	
item (3)			

Mark the following check-box if the certified copy of the earlier application is to be issued by the Office which for the purposes of the present international application is the receiving Office (a fee may be required):

☒ The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s) : (1) & (2)

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):* ISA / US

Earlier search *Fill in where a search (international, international-type or other) by the International Searching Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or the translation thereof) or by reference to the search request:*

Country (or regional Office):	Date *(day/month/year)*:	Number:
US	08 November 1996 (08.11.96)	08/747,112
	26 June 1997 (26.06.97)	60/050,809 (per postcard)

Box No. VIII CHECK LIST

This international application contains the following number of sheets:

1. request	: 6	sheets
2. description	: 57	sheets
3. claims	: 15	sheets
4. abstract	: 1	sheets
5. drawings	: 22	sheets
Total	: 101	sheets

This international application is accompanied by the item(s) marked below:

1. ☐ separate signed power of attorney
2. ☐ copy of general power of attorney
3. ☐ statement explaining lack of signature
4. ☐ priority document(s) *identified in Box No. VI as item(s):*
5. ☒ fee calculation sheet
6. ☐ separate indications concerning deposited microorganisms
7. ☐ nucleotide and/or amino acid sequence listing (diskette)
8. ☒ other *(specify)*: Transmittal Letter (dup)

Figure No. 1 of the drawings (if any) should accompany the abstract when it is published.

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Applicant:
PURDUE RESEARCH FOUNDATION
SEVICK-MURACA, Eva
PIERCE, Joseph
RICHTER, Steven
SHINDE, Rajesh
BALGI, Ganesh
KAO, Jeffery
JIANG, Huabei

Agent:
L Scott Paynter
(L. Scott PAYNTER)

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority specified by the applicant: ISA /	6. ☐ Transmittal of search copy delayed until search fee is paid

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

RECEIVED
MAY 4 1998
Woodard, Emhardt, Naughton, Moriarty & McNett

PCT/US97/20539

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

PAYNTER, L., Scott
Woodard, Emhardt, Naughton,
Moriarty & McNett
Bank One Center/Tower, Suite 3700
111 Monument Circle
Indianapolis, IN 46204
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 27 April 1998 (27.04.98)	
Applicant's or agent's file reference PUR-63/75P	**IMPORTANT NOTIFICATION**
International application No. PCT/US97/20539	**International filing date** (day/month/year) 07 November 1997 (07.11.97)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
KAO, Jeffery 301 Huckleberry Drive Lake Jackson, TX 77566 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [X] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
KAO, Jeffrey 301 Huckleberry Drive Lake Jackson, TX 77566 United States of America	US	US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[ ] the elected Offices concerned
[ ] other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Ingrid Hours Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 July 1998 (03.07.98)	
International application No. PCT/US97/20539	**Applicant's or agent's file reference** PUR-63/75P
International filing date (day/month/year) 07 November 1997 (07.11.97)	**Priority date** (day/month/year) 08 November 1996 (08.11.96)
Applicant SEVICK-MURACA, Eva et al	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   03 June 1998 (03.06.98)

   [ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was
   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland** Facsimile No.: (41-22) 740.14.35	Authorized officer S. De Michiel Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

RECEIVED

JUL 13 1998

Woodard, Emhardt, Naughton, Moriarty & McNett

PCT

From the INTERNATIONAL BUREAU

To:

PAYNTER, L., Scott
Woodard, Emhardt, Naughton,
Moriarty & McNett
Bank One Center/Tower, Suite 3700
111 Monument Circle
Indianapolis, IN 46204
ETATS-UNIS D'AMERIQUE

INFORMATION CONCERNING ELECTED OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

Date of mailing (day/month/year) 03 July 1998 (03.07.98)		
Applicant's or agent's file reference PUR-63/75P	**IMPORTANT INFORMATION**	
International application No. PCT/US97/20539	**International filing date** (day/month/year) 07 November 1997 (07.11.97)	**Priority date** (day/month/year) 08 November 1996 (08.11.96)
Applicant PURDUE RESEARCH FOUNDATION et al		

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

   AP :GH,KE,LS,MW,SD,SZ,UG,ZW
   EP :AT,BE,CH,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE
   National :AU,BG,BR,CA,CN,CZ,DE,GB,IL,JP,KP,KR,MN,NO,NZ,PL,RO,RU,SE,SK,US,
   VN

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

   EA :AM,AZ,BY,KG,KZ,MD,RU,TJ,TM
   OA :BF,BJ,CF,CG,CI,CM,GA,GN,ML,MR,NE,SN,TD,TG
   National :AL,AM,AT,AZ,BA,BB,BY,CH,CU,DK,EE,ES,FI,GE,GH,HU,ID,IS,KE,KG,KZ,
   LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MW,MX,PT,SD,SG,SI,SL,TJ,TM,TR,TT,UA,UG,UZ,
   YU,ZW

3. The applicant is reminded that he must enter the "national phase" **before the expiration of 30 months from the priority date** before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing , if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

   Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

   The entry into the European regional phase is postponed **until 31 months from the priority date** for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland** Facsimile No. (41-22) 740.14.35	Authorized officer: S. De Michiel Telephone No. (41-22) 338.83.38

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

L. SCOTT PAYNTER
WOODARD, EMHARDT, NAUGHTON, MORIARTY
BANK ONE CENTER/TOWER, SUITE 3700
111 MONUMENT CIRCLE
INDIANAPOLIS IN 46204

PCT

NOTIFICATION OF RECEIPT
OF DEMAND

(PCT Rule 61.1(b), first sentence
and Administrative Instructions, Section 601)

Date of mailing (day/month/year)	22 JUN 1998

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
PUR-63/75P	

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/US97/20539	07 NOV 97	08 NOV 96

Applicant
PURDUE RESEARCH FOUNDATION

1. The applicant is hereby notified that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

   03 June 1998 .

2. This date of receipt is:

   ☒ the actual date of receipt of the demand.

   ☐ the date on which the proper corrections to the demand were timely received.

3. ☐ This date is **AFTER** the expiration of 19 months from the priority date.

   Attention: The election(s) made in the demand does (do) not have the effect of postponing the commencement of the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22).

   For details, see Annex B to Form PCT/IB/301 sent by the International Bureau and Volume II of the PCT Applicant's Guide.

   ☐ This notification confirms the information given in person or by telephone on:

   ______________________ .

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/US	Authorized officer
Assistant Commissioner for Patents Box PCT Washington, D.C. 20231 Attn: IPEA/US	Stacia Sinnick for Paul Urrutia
Facsimile No.	Telephone No. (703) 305-3681

Form PCT/IPEA/402 (July 1992)

19

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PUR-63/75P	**FOR FURTHER ACTION** See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US97/20539	International filing date *(day/month/year)* 07 NOVEMBER 1997	Priority date *(day/month/year)* 08 NOVEMBER 1996
International Patent Classification (IPC) or national classification and IPC IPC(6): G01N 21/51 and US Cl.: 356/336		
Applicant PURDUE RESEARCH FOUNDATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   [x] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 20 sheets.

3. This report contains indications relating to the following items:

- I [X] Basis of the report
- II [ ] Priority
- III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV [ ] Lack of unity of invention
- V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI [ ] Certain documents cited
- VII [ ] Certain defects in the international application
- VIII [ ] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03 JUNE 1998	21 JANUARY 1999
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer RICHARD ROSENBERGER Telephone No. (703) 308-0956

Form PCT/IPEA/409 (cover sheet) (January 1994)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/20539

I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*:

☐ the international application as originally filed.

☒ the description, pages (See Attached) , as originally filed.
pages ________ , filed with the demand.
pages ________ , filed with the letter of ________.
pages ________ , filed with the letter of ________.

☒ the claims, Nos. (See Attached) , as originally filed.
Nos. ________ , as amended under Article 19.
Nos. ________ , filed with the demand.
Nos. ________ , filed with the letter of ________.
Nos. ________ , filed with the letter of ________.

☒ the drawings, sheets/~~fig~~ (See Attached) , as originally filed.
sheets/~~fig~~ ________ , filed with the demand.
sheets/~~fig~~ ________ , filed with the letter of ________.
sheets/~~fig~~ ________ , filed with the letter of ________.

2. The amendments have resulted in the cancellation of:

☒ the description, pages none.
☒ the claims, Nos. 36.
☒ the drawings, sheets/~~fig~~ none.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/20539

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	1-35, 37-50	YES
	Claims	none	NO
Inventive Step (IS)	Claims	1-35, 37-50	YES
	Claims	none	NO
Industrial Applicability (IA)	Claims	1-35, 37-50	YES
	Claims	none	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-35, 37-50 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest what is claimed. Although Paithankar et al teaches in general the use of multiple wavelength scattering measurement for determining size distributions, there is no disclosure therein relating to specific details of how to obtain such measurements from such measurements and of specific claimed details for making such measurements. For example, the reference does not teach a method in which isotropic scattering coefficient is calculated as a function of an estimate of the volume fraction and/or the size distribution (claims 1-7, 32-35, 37-40 and 46-50). The reference does not discuss the generation of the "comparisons signals" (claims 8-13). The reference does not disclose the making the calculations iteratively (claims 1-7, 14-18, and 22-24), nor the use of a P-Y (Perkus-Yervick) hard sphere model (claims 17, 25, 30-31, 40, 44, 48) nor of a Weibull distribution (claims 7, 18). The system of the reference does not disclose the use of a number of wavelengths "each being intensity-modulated at a predetermined frequency" and the detection signals "each being representative of at least one of a phase or an amplitude . . . relative to the predetermined frequency" (claims 19-25, and 37-39). The reference does not teach "determining the particle interaction parameter" (claims 13, 26-31 and 34-35), or the calculation of the isotropic scattering coefficient as a function of an estimate of the volume fraction and the size distribution (claim 36). The reference does not teach the use of a structure factor in the calculation (claims 41-45).

------------------- NEW CITATIONS -------------------

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/20539

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
pages, 1-29, 31-33, 36-38, 40-57, as originally filed.
pages, none, filed with the demand.
and additional amendments:
pages 30, 34, 35, 39, filed with the letter of 22 January 1999.

This report has been drawn on the basis of the claims,
numbers, none, as originally filed.
numbers, none, as amended under Article 19.
numbers, none , filed with the demand.
and additional amendments:
Claims 1-35, 37-50, filed with the letter of 22 January 1999.

This report has been drawn on the basis of the drawings,
sheets, 1-22, as originally filed.
sheets, none, filed with the demand.
and additional amendments:
NONE

where it is desired to minimize χ^2 so that it is less than or equal to an established error amount. Conditional 546 tests whether this minimization has taken place. If the minimum has been reached, then control flows to stage 550 and the estimate is provided as the measured product $\phi f(x)$. Subsequently, f(x) and ϕ may be separated by performing a summation approximation of $\int_0^\infty \phi f(x)dx = \phi$.

However, if conditional 546 is not satisfied, then control flows to stage 548 to improve the estimate of $\phi f(x)$. One embodiment for rapidly converging to the desired minimum error is through application of a Jacobian matrix relationship. Specifically, the product $\phi f(x)$ is divided into N number of bins representing $\phi f(x)_h$, where h = 1 to N. In order to update $\phi f(x)_h$ in each bin, the Jacobian matrix which describes the sensitivity of the isotropic scattering coefficient to changes in $\phi f(x)_h$ in each bin h and at each wavelength λ_j is computed. This Jacobian matrix is given by:

$$\Im = \begin{bmatrix} \frac{\partial(\mu'_s)^c_{\lambda_1}}{\partial(\phi f(x))_1} & \frac{\partial(\mu'_s)^c_{\lambda_1}}{\partial(\phi f(x))_2} & \cdots & \frac{\partial(\mu'_s)^c_{\lambda_1}}{\partial(\phi f(x))_N} \\ \frac{\partial(\mu'_s)^c_{\lambda_2}}{\partial(\phi f(x))_1} & \frac{\partial(\mu'_s)^c_{\lambda_2}}{\partial(\phi f(x))_2} & \cdots & \frac{\partial(\mu'_s)^c_{\lambda_2}}{\partial(\phi f(x))_N} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\partial(\mu'_s)^c_{\lambda_M}}{\partial(\phi f(x))_1} & \frac{\partial(\mu'_s)^c_{\lambda_M}}{\partial(\phi f(x))_2} & \cdots & \frac{\partial(\mu'_s)^c_{\lambda_M}}{\partial(\phi f(x))_N} \end{bmatrix} \qquad (10)$$

and each element is computed through a summation approximation of equation (3) with $\phi f(x)_h$ and $\phi f(x)_h + \Delta\phi f(x)_h$. The updates, $\delta\phi f(x)_h$, resulting from the differences between measured and computed isotropic scattering coefficients, can then be obtained from:

assuming an expected form of the PSD. Generally, particulate processes can usually be characterized by Gaussian or log-normal distributions, both of which can be represented by proper parametric choices for a Weibull distribution described as follows:

$$f(x) = \frac{c}{b}\left[\frac{(x-a)}{b}\right]^{c-a} \exp\left[-\left(\frac{x-a}{b}\right)^{c}\right] \qquad (15)$$

where a, b and c describe the peak location, width, and shape, respectively, of the distribution. For this embodiment, d corresponds to ϕ, and the equation (3) summation approximation becomes:

$$(\mu_s')_j^c = \sum_{i=1}^{z}\frac{3}{2}\frac{Q_{scat}(\lambda_j,n,x_i)}{x_i}\left(1-g(\lambda_j,n,x_i)\right)\left\{d\frac{c}{b}\left(\frac{x_i-a}{b}\right)^{(c-a)}\exp\left[-\left(\frac{x_i-a}{b}\right)^{c}\right]\right\}\Delta x \qquad (16)$$

where the expected range of particle diameter x from x_{min} to x_{max} is determined and incremented into k number of discrete sizes $x_i = x_{min} + (i-1)\,\Delta x$, $\Delta x = (x_{max} - x_{min}) / (z-1)$ for i=1 to z, and the terms $Q_{scat}(\lambda_j,n,x_i)$ and $g(\lambda_j,n,x_i)$ are determined from look-up tables based on λ_j, n, x_i.

Using Newton's method, the updates based estimation of the a,b,c,d parameters can be obtained from the resulting system of equations:

$$\Im^T\Im\Delta\zeta = \Im^T[(\mu_s')^o - (\mu_s')^c] \qquad (17)$$

where the Jacobian matrix $\Im$ now represents the sensitivity of isotropic scattering coefficients measured at wavelengths j=1,M upon the four parameters (a, b, c and d):

$$\Im = \begin{bmatrix} \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial a} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial b} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial c} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial d} \\ \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial a} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial b} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial c} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial d} \\ \frac{\partial(\mu_s' \vdots)^c_{\lambda_M}}{\partial a} & \frac{\partial(\mu_s' \vdots)^c_{\lambda_M}}{\partial b} & \frac{\partial(\mu_s' \vdots)^c_{\lambda_M}}{\partial c} & \frac{\partial(\mu_s' \vdots)^c_{\lambda_M}}{\partial d} \end{bmatrix} \quad (18)$$

The elements of the Jacobian are numerically computed using equation (3). The vectors, $(\mu_s')^o$ and $(\mu_s')^c$ contain the observed and computed values of isotropic scattering coefficients at the wavelengths of interest:

$$(\mu_s')^o = ((\mu_s')^o_{\lambda_1}, (\mu_s')^o_{\lambda_2}, \ldots (\mu_s')^o_{\lambda_M}), \qquad (\mu_s')^c = ((\mu_s')^c_{\lambda_1}, (\mu_s')^c_{\lambda_2}, \ldots (\mu_s')^c_{\lambda_M})$$

(19)

$\Delta\zeta$ is the vector updating the four parameters, a, b, c and d:

$$\Delta\zeta = (\delta a, \delta b, \delta c, \delta d)^T \qquad (20)$$

Thus, the particle sizing task now becomes to recover the four parameters (a, b, c and d) to describe f(x) and ϕ using the approach described in connection with loop 540.

In still another embodiment, a low pass filter is employed to smooth the estimate based on the parameters for an expected form of distribution, such as the Weibull distribution. In this embodiment, the size distribution is computed from the parameters and then subjected to a digital low pass filter by averaging over a window of $N^*\Delta x$.

$$f(x_p)^{new} = (1-\xi)f(x_p)^{old} + \frac{\xi}{N^*}\sum_{l=p-\frac{N^*}{2}}^{l=p+\frac{N^*}{2}} f(x_l)^{old} \qquad (21)$$

where ξ is a factor between 0 and 1, and the summation is over the N^*

intensity. In other embodiments of the present invention, the light source arrangement is configured to provide wavelengths and time-varying intensity suitable for interrogation of the particular process being monitored using techniques known to those skilled in the art.

Analyzer 150 also includes optical fiber 134 to detect re-emitted light from the particles in vessel 160 after multiple scattering. It is preferred that analyzer 150 be of rugged design suitable for industrial applications. Analyzer 150 includes a processor configured to execute software to determine values representative of PSD or volume fraction in accordance with the present invention. Furthermore, analyzer 150 is also operatively coupled to control elements 170 which are used to regulate processing in vessel 160. By way of non-limiting example, elements 170 may include valves, heaters, or agitation devices electronically regulated by analyzer 150. Analyzer 150 is further configured with appropriate programming and interfaces to provide one or more output signals to control elements 170 as a function of PSD or volume fraction. Thus, system 120 provides a closed loop feedback control system capability for regulating chemical processes from on-line measurement of PSD and/or volume fraction.

Systems 20 and 120 of FIGS. 1 and 3, respectively, are described with corresponding light source fibers 30, 130 and detecting fibers 36, 136 geometrically arranged to approximate infinite boundary conditions -- such that light travelling from fibers 30, 130 to fibers 36, 136 does not encounter a substantial boundary. Equations (6) or (7) are applied to determine the isotropic scattering coefficient μ_s' and the absorption μ_a under such infinite

CLAIMS

What is claimed is:

1. A method of particle analysis, comprising:

(a) exposing a number of particles in suspension to an incident light with a predetermined time-varying intensity, the particles being sufficiently close to one another to multiply scatter light;

(b) detecting multiply scattered light from the particles in response to the incident light to determine a first value corresponding to an observed isotropic scattering coefficient of the particles;

(c) establishing an estimate corresponding to at least one of volume fraction or size distribution of the particles;

(d) calculating a second value from the estimate, the second value corresponding to a calculated isotropic scattering coefficient;

(e) comparing the first and second values to establish an error;

(f) changing the estimate; and

(g) repeating said calculating, comparing, and changing until the error reaches a desired minimum.

2. The method of claim 1, wherein the incident light includes a number of different wavelengths of light, the first value is determined for each of the wavelengths, and said establishing, said calculating, said comparing, and said changing are performed for each of the different wavelengths.

3. The method of claim 1, further comprising controlling a process

as a function of the estimate and determining the estimate to generally maintain mass balance.

4. The method of claim 1, wherein the estimate corresponds to one of a number of parameters for an expected form of the size distribution.

5. The method of claim 4, wherein the incident light includes a number of different wavelengths of light, the first value is determined for each of the wavelengths, the parameters correspond to a Weibull distribution, and said calculating includes:

(i) establishing a number of particle size increments;

(ii) determining a scattering efficiency and a mean cosine of scattering angle as a function of the wavelengths and the increments; and

(iii) performing a first summation over a range of the particle sizes for each of the wavelengths, the first summation having the parameters, the scattering efficiency, and the mean cosine of scattering angle as arguments.

6. The method of claim 5, wherein said comparing includes performing a second summation over a range of the wavelengths, the second summation including a numerical difference between the first and second values as an argument.

7. The method of claim 5, wherein said changing includes updating the parameters as a function of the wavelengths, the first and second values,

and a third value corresponding to mass of the particles.

8. A system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light comprising:

a light source with a predetermined time-varying intensity configured to expose the medium to a number of different predetermined wavelengths of incident light;

a first sensor spaced apart from said source, said first sensor being configured to provide a first detection signal corresponding to detected light, the detected light being multiply scattered by the particles;

a processor responsive to the first detection signal and being configured to receive an exposure signal corresponding to said incident light, said processor being configured to generate: (a) a number of comparison signals each corresponding to a difference with respect to time between the detected light and the incident light for a corresponding one of the wavelengths, (b) a number of scattering signals each correspondingly determined from the comparison signals and each corresponding to an observed isotropic scattering coefficient of the medium for a different one of the wavelengths, and (c) an output signal indicative of one of size distribution or volume fraction of the particles, said output signal being determined as a function of said scattering signals; and

an output device responsive to said output signal to provide an output corresponding to the size distribution or volume fraction of the particles.

9. The system of claim 8, further comprising a reaction vessel containing the particles and medium, and wherein said output device includes a control element operatively coupled to said reaction vessel and responsive to said output to regulate a process involving the particles.

10. The system of claim 8, wherein said processor is further configured to determine said size distribution or volume fraction as a function of mass of the particles.

11. The system of claim 8, further comprising a second sensor providing a second detection signal, said comparison signals being determined as a function of said first and second detection signals for each of the wavelengths.

12. The system of claim 8, wherein said processor further determines a structure factor indicative of particle-to-particle interactions, said structure factor varying in accordance with concentration of the particles in the medium.

13. The system of claim 8, wherein said processor is configured to generate a particle interaction signal representative of particle-to-particle interactions that vary with particle concentration and influence light scattering behavior of the particles.

14. A system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light, comprising:

(a) a light source with a predetermined time-varying intensity configured to expose the medium to a number of different wavelengths of light;

(b) a sensor spaced apart from said source, said sensor being configured to provide a detected light signal corresponding to multiply scattered light from the particles at the different wavelengths in response to exposure to said source;

(c) a processor responsive to said detected light signal, said processor including a calculation means for generating an output signal corresponding to at least one of particle size distribution, particle volume fraction, or a structure factor determined in accordance with an observed isotropic scattering coefficient of the medium, said structure factor being representative of particle interactions that influence light scattering behavior of said particles, said processor being configured to determine a value representative of said observed isotropic scattering coefficient from said detected light signal; and

(d) an output device responsive to said output signal to provide an output corresponding to said at least one of said particle size distribution, said particle volume fraction, or said structure factor of the particles.

15. The system of claim 14, further comprising a reaction vessel containing the particles and the medium, and wherein said output device includes a control element operatively coupled to said reaction vessel and

responsive to said output to regulate a reaction involving the particles.

16. The system of claim 14, wherein said calculation means includes an estimating means for iteratively determining said size distribution or said volume fraction as a function of mass of the particles.

17. The system of claim 14, wherein said structure factor is dependent on said particle size distribution and said particle volume fraction, and corresponds to a P-Y hard sphere model.

18. The system of claim 14, wherein said calculation means includes a number of parameters corresponding to a Weibull distribution.

19. A method of particle analysis, comprising:

(a) exposing a medium with a number of suspended particles to a number of light wavelengths, the wavelengths each being intensity-modulated at a predetermined frequency;

(b) detecting multiply scattered light from the medium in response to said exposing to characterize propagation of the multiply scattered light through the medium with a number of values, the values each corresponding to a different one of the wavelengths and each being representative of at least one of a phase or an amplitude of the multiply scattered light relative to the predetermined frequency; and

(c) providing an output determined from the values, the output

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corresponding to at least one of a particle size distribution, particle volume fraction, or a particle interaction parameter, the particle interaction parameter corresponding to a nonlinear relationship between particle concentration and an isotropic scattering coefficient for the particles.

20. The method of claim 19, further comprising controlling a process in accordance with the output.

21. The method of claim 19, wherein said providing includes determining the observed isotropic scattering coefficient and an absorption coefficient for the particles for each of the wavelengths from a corresponding one of the values.

22. The method of claim 19, wherein said providing includes:

(i) determining an observed isotropic scattering coefficient for the particles for each of the wavelengths from a corresponding one of the values;

(ii) establishing an estimate corresponding to at least one of the size distribution or the volume fraction;

(iii) determining a calculated isotropic scattering coefficient for each of the wavelengths from the estimate;

(iv) comparing the observed and calculated isotropic scattering coefficients to establish an error;

(v) changing the estimate; and

(vi) repeating said calculating, comparing, and changing until the

error reaches a desired minimum.

23. The method of claim 22, wherein said providing includes selecting the estimate to generally maintain mass balance of the particles, and the estimate corresponds to an expected form of the size distribution of the particles.

24. The method of claim 22, wherein the calculated isotropic scattering coefficient is determined with an equation having an estimated product of the size distribution and the volume fraction as an argument.

25. The method of claim 19, wherein the particle interaction parameter is determined from a P-Y structure factor model.

26. A method of particle analysis, comprising:

(a) exposing a number of particles to a number of light wavelengths of predetermined time-varying intensity;

(b) detecting multiply scattered light from the particles in response to said exposing to determine a number of values each corresponding to a different one of the wavelengths, the values each being representative of a time-of-flight characteristic of the particles; and

(c) providing an output determined from the values, the output corresponding to at least one of a particle size distribution, particle volume fraction, or a particle interaction parameter, the particle interaction parameter

corresponding to a nonlinear relationship between particle concentration and an isotropic scattering coefficient for the particles.

27. The method of claim 26, wherein the particles are suspended in a fluid medium and further comprising controlling a process in accordance with the output.

28. The method of claim 26, wherein the particles have a concentration in the fluid medium of at least about 10% by volume.

29. The method of claim 26, wherein said determining includes calculating at least one of volume fraction and size distribution of the particles in the fluid.

30. The method of claim 26, wherein the particle interaction parameter is determined from the Percus-Yevick hard sphere model.

31. The method of claim 30, wherein said calculating includes adjusting the hard sphere model to account for forces between the particles.

32. A method of analysis, comprising:

(a) exposing a fluid to an incident light, the fluid having a number of suspended particles therein, the suspended particles being sufficiently concentrated in the fluid to scatter light;

(b) detecting multiply scattered light in response to said exposing to determine a time-based value characteristic of propagation time of the multiply scattered light through the fluid;

(c) determining a quantity as a function of the value, the quantity corresponding to an isotropic scattering coefficient; and

(d) providing an output determined from the quantity, the output corresponding to at least one of particle volume fraction, particle size distribution, or a particle interaction parameter, the particle interaction parameter corresponding to particle-to-particle interactions influencing light scattering behavior of the particles.

33. The method of claim 32, further comprising controlling a process in which the particles are altered by utilizing the output as a feedback variable.

34. The method of claim 32, wherein said providing includes establishing an estimate corresponding to volume fraction and the size distribution and determining the particle interaction parameter as a function of the estimate.

35. The method of claim 34, further comprising constraining the estimate to maintain mass balance.

36. The method of claim 32, wherein said providing includes

calculating a number corresponding to the isotropic scattering coefficient as a function of an estimate of the volume fraction and the size distribution.

37. The method of claim 32, wherein the incident light is intensity modulated at a predetermined frequency, and said determining includes comparing the incident light and the scattered light to determine the value, and the value is representative of a relative phase or amplitude of the scattered light for the predetermined frequency.

38. The method of claim 37, wherein said detecting includes detecting the scattered light with a second sensor spaced apart from the first sensor by a separation distance and said determining includes calculating the quantity in accordance with the separation distance.

39. The method of claim 37, wherein said providing includes determining the volume fraction or size distribution in accordance with the diffusion equation for multiply scattered light.

40. The method of claim 32, wherein the particle interaction parameter is determined from a P-Y structure factor model.

41. A system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light, comprising:

a light source configured to expose the medium to a number of

different predetermined wavelengths of incident light each having a predetermined time-varying intensity;

a first sensor spaced apart from said source, said first sensor being configured to provide a first detection signal corresponding to detected light, the detected light being multiply scattered by the particles;

a processor responsive to said first detection signal and being configured to receive an exposure signal corresponding to said incident light, said processor being configured to generate: (a) a number of propagation signals by comparing said first detection signal and said exposure signal for each of said wavelengths, said propagation signals each characterizing time of flight of the detected light through the medium resulting from multiple scattering by the particles for a corresponding one of said wavelengths, (b) a number of scattering signals each corresponding to an isotropic scattering coefficient of the medium and being determined from a corresponding one of said propagation signals, and (c) an output signal indicative of at least one of size distribution or volume fraction of the particles, said output signal being determined from said scattering signals and a structure factor, said structure factor accounting for particle-to-particle interactions influencing light scattering behavior of the particles; and

an output device responsive to said output signal to provide an output corresponding to said size distribution or said volume fraction of the particles.

42. The system of claim 41, wherein said processor is further configured to determine said size distribution or said volume fraction as a

function of mass of the particles.

43. The system of claim 41, further comprising a second sensor providing a second detection signal, said scattering signals being determined as a function of said first and second detection signals for each of the wavelengths.

44. The system of claim 41, wherein said structure factor corresponds to a P-Y hard sphere structure factor model.

45. The system of claim 41, wherein said processor further generates an absorption signal corresponding to an absorption coefficient of the medium and determines said absorption signal from said propagation signal.

46. A method of particle analysis, comprising:

(a) exposing a number of particles to a number of light wavelengths of predetermined time-varying intensity;

(b) detecting multiply scattered light from the particles in response to said exposing to determine a number of time-based propagation characteristics of the particles each corresponding to a different one of the wavelengths; and

(c) calculating an observed isotropic scattering coefficient for each of the wavelengths from the characteristics;

(d) determining a calculated isotropic scattering coefficient for each of the wavelengths from an estimate of at least one of particle size distribution or particle volume fraction;

(e) comparing the observed isotropic scattering coefficient and calculated isotropic scattering coefficient for each of the wavelengths to establish and error;

(f) adjusting the estimate and repeating said determining and said comparing until the error reaches a desired minimum; and

(g) providing an output corresponding to at least one of the particle size distribution, particle volume fraction, or a particle interaction parameter.

47. The method of claim 46, wherein said determining includes establishing the particle interaction parameter as a function of the particle volume fraction and the particle size distribution.

48. The method of claim 47, wherein the particle interaction parameter corresponds to the P-Y hard sphere structure factor.

49. The method of claim 48, wherein the calculated isotropic scattering coefficient is determined with an equation having the structure factor and an estimated product of the size distribution and the volume fraction as arguments.

50. The method of claim 46, wherein the particles include liquid

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droplets dispersed in a fluid medium, the droplets and the medium having different indices of refraction.

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FEB 17 1999

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: L. SCOTT PAYNTER
WOODARD, EMHARDT, NAUGHTON, MORIARTY & MCNETT
BANK ONE CENTER/TOWER, SUITE 3700
111 MONUMENT CIRCLE
INDIANAPOLIS, INDIANA 46204

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing (day/month/year): 12 FEB 1999

IMPORTANT NOTIFICATION

Applicant's or agent's file reference PUR-63/75P		
International application No. PCT/US97/20539	International filing date *(day/month/year)* 07 NOVEMBER 1997	Priority Date *(day/month/year)* 08 NOVEMBER 1996
Applicant PURDUE RESEARCH FOUNDATION		

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-	Authorized officer RICHARD ROSENBERGER

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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PUR-63/75P	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US97/20539	International filing date *(day/month/year)* 07 NOVEMBER 1997	Priority date *(day/month/year)* 08 NOVEMBER 1996

International Patent Classification (IPC) or national classification and IPC
IPC(6): G01N 21/51 and US Cl.: 356/336

Applicant
PURDUE RESEARCH FOUNDATION

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   ☑ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 20 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 03 JUNE 1998	Date of completion of this report 21 JANUARY 1999
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer RICHARD ROSENBERGER Telephone No. (703) 308-0956

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/20539

I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*:

☐ the international application as originally filed.

☒ the description, pages (See Attached), as originally filed.
pages ______, filed with the demand.
pages ______, filed with the letter of ______.
pages ______, filed with the letter of ______.

☒ the claims, Nos. (See Attached), as originally filed.
Nos. ______, as amended under Article 19.
Nos. ______, filed with the demand.
Nos. ______, filed with the letter of ______.
Nos. ______, filed with the letter of ______.

☒ the drawings, sheets/~~fig~~ (See Attached), as originally filed.
sheets/~~fig~~ ______, filed with the demand.
sheets/~~fig~~ ______, filed with the letter of ______.
sheets/~~fig~~ ______, filed with the letter of ______.

2. The amendments have resulted in the cancellation of:

☒ the description, pages none.

☒ the claims, Nos. 36.

☒ the drawings, sheets/~~fig~~ none.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/20539

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	1-35, 37-50	YES
	Claims	none	NO
Inventive Step (IS)	Claims	1-35, 37-50	YES
	Claims	none	NO
Industrial Applicability (IA)	Claims	1-35, 37-50	YES
	Claims	none	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-35, 37-50 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest what is claimed. Although Paithankar et al teaches in general the use of multiple wavelength scattering measurement for determining size distributions, there is no disclosure therein relating to specific details of how to obtain such measurements from such measurements and of specific claimed details for making such measurements. For example, the reference does not teach a method in which isotropic scattering coefficient is calculated as a function of an estimate of the volume fraction and/or the size distribution (claims 1-7, 32-35, 37-40 and 46-50). The reference does not discuss the generation of the "comparisons signals" (claims 8-13). The reference does not disclose the making the calculations iteratively (claims 1-7, 14-18, and 22-24), nor the use of a P-Y (Perkus-Yervick) hard sphere model (claims 17, 25, 30-31, 40, 44, 48) nor of a Weibull distribution (claims 7, 18). The system of the reference does not disclose the use of a number of wavelengths "each being intensity-modulated at a predetermined frequency" and the detection signals "each being representative of at least one of a phase or an amplitude . . . relative to the predetermined frequency" (claims 19-25, and 37-39). The reference does not teach "determining the particle interaction parameter" (claims 13, 26-31 and 34-35), or the calculation of the isotropic scattering coefficient as a function of an estimate of the volume fraction and the size distribution (claim 36). The reference does not teach the use of a structure factor in the calculation (claims 41-45).

------------------- NEW CITATIONS -------------------
NONE

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
pages, 1-29, 31-33, 36-38, 40-57, as originally filed.
pages, none, filed with the demand.
and additional amendments:
pages 30, 34, 35, 39, filed with the letter of 22 January 1999.

This report has been drawn on the basis of the claims,
numbers, none, as originally filed.
numbers, none, as amended under Article 19.
numbers, none , filed with the demand..
and additional amendments:
Claims 1-35, 37-50, filed with the letter of 22 January 1999.

This report has been drawn on the basis of the drawings,
sheets, 1-22, as originally filed.
sheets, none, filed with the demand.
and additional amendments:
NONE

where it is desired to minimize χ^2 so that it is less than or equal to an established error amount. Conditional 546 tests whether this minimization has taken place. If the minimum has been reached, then control flows to stage 550 and the estimate is provided as the measured product $\phi f(x)$. Subsequently, f(x) and ϕ may be separated by performing a summation approximation of $\int_0^\infty \phi f(x)dx = \phi$.

However, if conditional 546 is not satisfied, then control flows to stage 548 to improve the estimate of $\phi f(x)$. One embodiment for rapidly converging to the desired minimum error is through application of a Jacobian matrix relationship. Specifically, the product $\phi f(x)$ is divided into N number of bins representing $\phi f(x)_h$, where h = 1 to N. In order to update $\phi f(x)_h$ in each bin, the Jacobian matrix which describes the sensitivity of the isotropic scattering coefficient to changes in $\phi f(x)_h$ in each bin h and at each wavelength λ_i is computed. This Jacobian matrix is given by:

$$\mathfrak{J} = \begin{bmatrix} \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial(\phi f(x))_1} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial(\phi f(x))_2} & \cdots & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial(\phi f(x))_N} \\ \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial(\phi f(x))_1} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial(\phi f(x))_2} & \cdots & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial(\phi f(x))_N} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\partial(\mu_s')^c_{\lambda_M}}{\partial(\phi f(x))_1} & \frac{\partial(\mu_s')^c_{\lambda_M}}{\partial(\phi f(x))_2} & \cdots & \frac{\partial(\mu_s')^c_{\lambda_M}}{\partial(\phi f(x))_N} \end{bmatrix} \quad (10)$$

and each element is computed through a summation approximation of equation (3) with $\phi f(x)_h$ and $\phi f(x)_h + \Delta\phi f(x)_h$. The updates, $\delta\phi f(x)_h$, resulting from the differences between measured and computed isotropic scattering coefficients, can then be obtained from:

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assuming an expected form of the PSD. Generally, particulate processes can usually be characterized by Gaussian or log-normal distributions, both of which can be represented by proper parametric choices for a Weibull distribution described as follows:

$$f(x) = \frac{c}{b}\left[\frac{(x-a)}{b}\right]^{c-1}\exp\left[-\left(\frac{x-a}{b}\right)^{c}\right] \qquad (15)$$

where a, b and c describe the peak location, width, and shape, respectively, of the distribution. For this embodiment, d corresponds to ϕ, and the equation (3) summation approximation becomes:

$$(\mu_s')_j = \sum_{i=1}^{z}\frac{3}{2}\frac{Q_{scat}(\lambda_j, n, x_i)}{x_i}\left(1-g(\lambda_j, n, x_i)\right)\left\{d\frac{c}{b}\left(\frac{x_i-a}{b}\right)^{(c-1)}\exp\left[-\left(\frac{x_i-a}{b}\right)^{c}\right]\right\}\Delta x$$

(16)

where the expected range of particle diameter x from x_{min} to x_{max} is determined and incremented into k number of discrete sizes $x_i = x_{min} + (i-1)\,\Delta x$, $\Delta x = (x_{max} - x_{min}) / (z-1)$ for i=1 to z, and the terms $Q_{scat}(\lambda_j, n, x_i)$ and $g(\lambda_j, n, x_i)$ are determined from look-up tables based on λ_j, n, x_i.

Using Newton's method, the updates based estimation of the a,b,c,d parameters can be obtained from the resulting system of equations:

$$\mathfrak{J}^T\mathfrak{J}\Delta\zeta = \mathfrak{J}^T[(\mu_s')^m - (\mu_s')^c] \qquad (17)$$

where the Jacobian matrix $\mathfrak{J}$ now represents the sensitivity of isotropic scattering coefficients measured at wavelengths j=1,M upon the four parameters (a, b, c and d)

AMENDED SHEET

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$$\mathfrak{J} = \begin{bmatrix} \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial a} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial b} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial c} & \frac{\partial(\mu_s')^c_{\lambda_1}}{\partial d} \\ \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial a} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial b} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial c} & \frac{\partial(\mu_s')^c_{\lambda_2}}{\partial d} \\ \vdots & \vdots & \vdots & \vdots \\ \frac{\partial(\mu_s')^c_{\lambda_M}}{\partial a} & \frac{\partial(\mu_s')^c_{\lambda_M}}{\partial b} & \frac{\partial(\mu_s')^c_{\lambda_M}}{\partial c} & \frac{\partial(\mu_s')^c_{\lambda_M}}{\partial d} \end{bmatrix} \qquad (18)$$

The elements of the Jacobian are numerically computed using equation (3). The vectors, $(\mu_s')^o$ and $(\mu_s')^c$ contain the observed and computed values of isotropic scattering coefficients at the wavelengths of interest:

$$(\mu_s')^o = ((\mu_s')^o_{\lambda_1}, (\mu_s')^o_{\lambda_2}, \ldots (\mu_s')^o_{\lambda_M}) \qquad (\mu_s')^c = ((\mu_s')^c_{\lambda_1}, (\mu_s')^c_{\lambda_2}, \ldots (\mu_s')^c_{\lambda_M}) \qquad (19)$$

$\Delta\zeta$ is the vector updating the four parameters, a, b, c and d:

$$\Delta\zeta = (\delta a, \delta b, \delta c, \delta d)^T \qquad (20)$$

Thus, the particle sizing task now becomes to recover the four parameters (a, b, c and d) to describe f(x) and ϕ using the approach described in connection with loop 540.

In still another embodiment, a low pass filter is employed to smooth the estimate based on the parameters for an expected form of distribution, such as the Weibull distribution. In this embodiment, the size distribution is computed from the parameters and then subjected to a digital low pass filter by averaging over a window of $N^*\Delta x$.

$$f(x_p)^{new} = (1-\xi)f(x_p)^{old} + \frac{\xi}{N^*}\sum_{l=p-\frac{N^*}{2}}^{l=p+\frac{N^*}{2}} f(x_l)^{old} \qquad (21)$$

where ξ is a factor between 0 and 1, and the summation is over the N^*

intensity. In other embodiments of the present invention, the light source arrangement is configured to provide wavelengths and time-varying intensity suitable for interrogation of the particular process being monitored using techniques known to those skilled in the art.

Analyzer 150 also includes optical fiber 134 to detect re-emitted light from the particles in vessel 160 after multiple scattering. It is preferred that analyzer 150 be of rugged design suitable for industrial applications. Analyzer 150 includes a processor configured to execute software to determine values representative of PSD or volume fraction in accordance with the present invention. Furthermore, analyzer 150 is also operatively coupled to control elements 170 which are used to regulate processing in vessel 160. By way of non-limiting example, elements 170 may include valves, heaters, or agitation devices electronically regulated by analyzer 150. Analyzer 150 is further configured with appropriate programming and interfaces to provide one or more output signals to control elements 170 as a function of PSD or volume fraction. Thus, system 120 provides a closed loop feedback control system capability for regulating chemical processes from on-line measurement of PSD and/or volume fraction.

Systems 20 and 120 of FIGS. 1 and 3, respectively, are described with corresponding light source fibers 30, 130 and detecting fibers 36, 136 geometrically arranged to approximate infinite boundary conditions -- such that light travelling from fibers 30, 130 to fibers 36, 136 does not encounter a substantial boundary. Equations (6) or (7) are applied to determine the isotropic scattering coefficient μ_s' and the absorption μ_a under such infinite

CLAIMS

What is claimed is:

1. A method of particle analysis, comprising:

(a) exposing a number of particles in suspension to an incident light with a predetermined time-varying intensity, the particles being sufficiently close to one another to multiply scatter light;

(b) detecting multiply scattered light from the particles in response to the incident light to determine a first value corresponding to an observed isotropic scattering coefficient of the particles;

(c) establishing an estimate corresponding to at least one of volume fraction or size distribution of the particles;

(d) calculating a second value from the estimate, the second value corresponding to a calculated isotropic scattering coefficient;

(e) comparing the first and second values to establish an error;

(f) changing the estimate; and

(g) repeating said calculating, comparing, and changing until the error reaches a desired minimum.

2. The method of claim 1, wherein the incident light includes a number of different wavelengths of light, the first value is determined for each of the wavelengths, and said establishing, said calculating, said comparing, and said changing are performed for each of the different wavelengths.

3. The method of claim 1, further comprising controlling a process as a function of the estimate and determining the estimate to generally maintain mass balance.

4. The method of claim 1, wherein the estimate corresponds to one of a number of parameters for an expected form of the size distribution.

5. The method of claim 4, wherein the incident light includes a number of different wavelengths of light, the first value is determined for each of the wavelengths, the parameters correspond to a Weibull distribution, and said calculating includes:

(i) establishing a number of particle size increments;

(ii) determining a scattering efficiency and a mean cosine of scattering angle as a function of the wavelengths and the increments; and

(iii) performing a first summation over a range of the particle sizes for each of the wavelengths, the first summation having the parameters, the scattering efficiency, and the mean cosine of scattering angle as arguments.

6 The method of claim 5, wherein said comparing includes performing a second summation over a range of the wavelengths, the second summation including a numerical difference between the first and second

values as an argument.

7. The method of claim 5, wherein said changing includes updating the parameters as a function of the wavelengths, the first and second values, and a third value corresponding to mass of the particles.

8. A system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light comprising:

a light source with a predetermined time-varying intensity configured to expose the medium to a number of different predetermined wavelengths of incident light;

a first sensor spaced apart from said source, said first sensor being configured to provide a first detection signal corresponding to detected light, the detected light being multiply scattered by the particles;

a processor responsive to the first detection signal and being configured to receive an exposure signal corresponding to said incident light, said processor being configured to generate: (a) a number of comparison signals each corresponding to a difference with respect to time between the detected light and the incident light for a corresponding one of the wavelengths, (b) a number of scattering signals each correspondingly determined from the comparison signals and each corresponding to an observed isotropic scattering coefficient of the medium for a different one of

the wavelengths, and (c) an output signal indicative of one of size distribution or volume fraction of the particles, said output signal being determined as a function of said scattering signals; and

an output device responsive to said output signal to provide an output corresponding to the size distribution or volume fraction of the particles.

9. The system of claim 8, further comprising a reaction vessel containing the particles and medium, and wherein said output device includes a control element operatively coupled to said reaction vessel and responsive to said output to regulate a process involving the particles.

10. The system of claim 8, wherein said processor is further configured to determine said size distribution or volume fraction as a function of mass of the particles.

11. The system of claim 8, further comprising a second sensor providing a second detection signal, said comparison signals being determined as a function of said first and second detection signals for each of the wavelengths.

12 The system of claim 8, wherein said processor further determines a structure factor indicative of particle-to-particle interactions,

said structure factor varying in accordance with concentration of the particles in the medium.

13. The system of claim 8, wherein said processor is configured to generate a particle interaction signal representative of particle-to-particle interactions that vary with particle concentration and influence light scattering behavior of the particles.

14. A system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light, comprising:

(a) a light source with a predetermined time-varying intensity configured to expose the medium to a number of different wavelengths of light;

(b) a sensor spaced apart from the source, said sensor being configured to provide a detected light signal corresponding to multiply scattered light from the particles at the different wavelengths in response to exposure to said source;

(c) a processor responsive to said detected light signal, said processor including a calculation means for generating an output signal corresponding to at least one of particle size distribution or volume fraction in accordance with an observed isotropic scattering coefficient of the medium determined from said detected light signal, said calculation means including a means for iteratively determining a structure factor from an estimate corresponding to at least one of

said particle size distribution or said volume fraction, said structure factor being representative of particle interactions that influence light scattering behavior of said particles; and

(d) an output device responsive to said output signal to provide an output corresponding to at least one of said size distribution or said volume fraction.

15. The system of claim 14, further comprising a reaction vessel containing the particles and the medium, and wherein said output device includes a control element operatively coupled to said reaction vessel and responsive to said output to regulate a reaction involving the particles.

16. The system of claim 14, wherein said calculation means includes an estimating means for iteratively determining said size distribution or said volume fraction as a function of mass of the particles.

17. The system of claim 14, wherein said structure factor is dependent on said particle size distribution and said particle volume fraction, and corresponds to a P-Y hard sphere model.

18. The system of claim 14, wherein said calculation means includes a number of parameters corresponding to a Weibull distribution.

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19. A method of particle analysis, comprising:

(a) exposing a medium with a number of suspended particles to a number of light wavelengths, the wavelengths each being intensity-modulated at a predetermined frequency;

(b) detecting multiply scattered light from the medium in response to said exposing to characterize propagation of the multiply scattered light through the medium with a number of values, the values each corresponding to a different one of the wavelengths and each being representative of at least one of a phase or an amplitude of the multiply scattered light relative to the predetermined frequency; and

(c) providing an output determined from the values, the output corresponding to at least one of a particle size distribution, particle volume fraction, or a particle interaction parameter, the particle interaction parameter corresponding to a nonlinear relationship between particle concentration and an isotropic scattering coefficient for the particles.

20. The method of claim 19, further comprising controlling a process in accordance with the output.

21. The method of claim 19, wherein said providing includes determining the observed isotropic scattering coefficient and an absorption

coefficient for the particles for each of the wavelengths from a corresponding one of the values.

22. The method of claim 19, wherein said providing includes:

(i) determining an observed isotropic scattering coefficient for the particles for each of the wavelengths from a corresponding one of the values;

(ii) establishing an estimate corresponding to at least one of the size distribution or the volume fraction;

(iii) determining a calculated isotropic scattering coefficient for each of the wavelengths from the estimate;

(iv) comparing the observed and calculated isotropic scattering coefficients to establish an error;

(v) changing the estimate; and

(vi) repeating said calculating, comparing, and changing until the error reaches a desired minimum.

23. The method of claim 22, wherein said providing includes selecting the estimate to generally maintain mass balance of the particles, and the estimate corresponds to an expected form of the size distribution of the particles

24. The method of claim 22, wherein the calculated isotropic

scattering coefficient is determined with an equation having an estimated product of the size distribution and the volume fraction as an argument.

25. The method of claim 19, wherein the particle interaction parameter is determined from a P-Y structure factor model.

26. A method of particle analysis, comprising:

(a) exposing a number of particles to a number of light wavelengths of predetermined time-varying intensity;

(b) detecting multiply scattered light from the particles in response to said exposing to determine a number of values each corresponding to a different one of the wavelengths, the values each being representative of a time-of-flight characteristic of the particles; and

(c) providing an output determined from the values, the output corresponding to at least one of a particle size distribution or volume fraction and being determined in accordance with a particle interaction parameter, the particle interaction parameter being representative of a nonlinear relationship between particle concentration and an isotropic scattering coefficient for the particles.

27. The method of claim 26, wherein the particles are suspended in a fluid medium and further comprising controlling a process in accordance with the output.

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28. The method of claim 26, wherein the particles have a concentration in the fluid medium of at least about 10% by volume.

29. The method of claim 26, wherein said determining includes calculating at least one of volume fraction and size distribution of the particles in the fluid.

30. The method of claim 26, wherein the particle interaction parameter is determined from the Percus-Yevick hard sphere model.

31. The method of claim 30, wherein said calculating includes adjusting the hard sphere model to account for forces between the particles.

32. A method of analysis, comprising:

(a) exposing a fluid to an incident light, the fluid having a number of suspended particles therein, the suspended particles being sufficiently concentrated in the fluid to scatter light;

(b) detecting multiply scattered light in response to said exposing to determine a time-based value characteristic of propagation time of the multiply scattered light through the fluid;

(c) determining a quantity as a function of the value, the quantity corresponding to an isotropic scattering coefficient; and

(d) providing an output corresponding to at least one of volume

fraction, particle size distribution, or a particle interaction parameter, the particle interaction parameter corresponding to particle-to-particle interactions influencing light scattering behavior of the particles, said providing including calculating a number representative of the isotropic scattering coefficient as a function of an estimate corresponding to the volume fraction and the size distribution.

33. The method of claim 32, further comprising controlling a process in which the particles are altered by utilizing the output as a feedback variable.

34. The method of claim 32, wherein said providing includes establishing an estimate corresponding to volume fraction and the size distribution and determining the particle interaction parameter as a function of the estimate.

35. The method of claim 34, further comprising constraining the estimate to maintain mass balance.

37. The method of claim 32, wherein the incident light is intensity modulated at a predetermined frequency, and said determining includes comparing the incident light and the scattered light to determine the value, and the value is representative of a relative phase or amplitude of the scattered light for the predetermined frequency.

38. The method of claim 37, wherein said detecting includes detecting the scattered light with a second sensor spaced apart from the first sensor by a separation distance and said determining includes calculating the quantity in accordance with the separation distance.

39. The method of claim 37, wherein said providing includes determining the volume fraction or size distribution in accordance with the diffusion equation for multiply scattered light.

40. The method of claim 32, wherein the particle interaction parameter is determined from a P-Y structure factor model.

41. A system for analyzing a number of particles suspended in a medium in sufficient concentration to multiply scatter light, comprising:

a light source configured to expose the medium to a number of

different predetermined wavelengths of incident light each having a predetermined time-varying intensity;

a first sensor spaced apart from said source, said first sensor being configured to provide a first detection signal corresponding to detected light, the detected light being multiply scattered by the particles;

a processor responsive to said first detection signal and being configured to receive an exposure signal corresponding to said incident light, said processor being configured to generate: (a) a number of propagation signals by comparing said first detection signal and said exposure signal for each of said wavelengths, said propagation signals each characterizing time of flight of the detected light through the medium resulting from multiple scattering by the particles for a corresponding one of said wavelengths, (b) a number of scattering signals each corresponding to an isotropic scattering coefficient of the medium and being determined from a corresponding one of said propagation signals, and (c) an output signal indicative of at least one of size distribution or volume fraction of the particles, said output signal being determined from said scattering signals and a structure factor, said structure factor accounting for particle-to-particle interactions influencing light scattering behavior of the particles; and

an output device responsive to said output signal to provide an output corresponding to said size distribution or said volume fraction of the particles.

42. The system of claim 41, wherein said processor is further configured to determine said size distribution or said volume fraction as a function of mass of the particles.

43. The system of claim 41, further comprising a second sensor providing a second detection signal, said scattering signals being determined as a function of said first and second detection signals for each of the wavelengths.

44. The system of claim 41, wherein said structure factor corresponds to a P-Y hard sphere structure factor model.

45. The system of claim 41, wherein said processor further generates an absorption signal corresponding to an absorption coefficient of the medium and determines said absorption signal from said propagation signal.

46. A method of particle analysis, comprising:

(a) exposing a number of particles to a number of light wavelengths of predetermined time-varying intensity;

(b) detecting multiply scattered light from the particles in response to said exposing to determine a number of time-based propagation

characteristics of the particles each corresponding to a different one of the wavelengths; and

(c) calculating an observed isotropic scattering coefficient for each of the wavelengths from the characteristics;

(d) determining a calculated isotropic scattering coefficient for each of the wavelengths from an estimate of at least one of particle size distribution or particle volume fraction;

(e) comparing the observed isotropic scattering coefficient and calculated isotropic scattering coefficient for each of the wavelengths to establish and error;

(f) adjusting the estimate and repeating said determining and said comparing until the error reaches a desired minimum; and

(g) providing an output corresponding to at least one of the particle size distribution, particle volume fraction, or a particle interaction parameter.

47. The method of claim 46, wherein said determining includes establishing the particle interaction parameter as a function of the particle volume fraction and the particle size distribution.

48. The method of claim 47, wherein the particle interaction parameter corresponds to the P-Y hard sphere structure factor.

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49. The method of claim 48, wherein the calculated isotropic scattering coefficient is determined with an equation having the structure factor and an estimated product of the size distribution and the volume fraction as arguments.

50. The method of claim 46, wherein the particles include liquid droplets dispersed in a fluid medium, the droplets and the medium having different indices of refraction.

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Woodard, Emhardt, Naughton, Moriarty & McNett

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From the INTERNATIONAL BUREAU

To:

PAYNTER, L., Scott
Woodard, Emhardt, Naughton,
Moriarty & McNett
Bank One Center/Tower, Suite 3700
111 Monument Circle
Indianapolis, IN 46204
ETATS-UNIS D'AMERIQUE

NOTIFICATION CONCERNING SUBMISSION OF PRIORITY DOCUMENTS

(PCT Administrative Instructions, Section 411)

Date of mailing (day/month/year) 09 March 1998 (09.03.98)		
Applicant's or agent's file reference PUR-63/75P	IMPORTANT NOTIFICATION	
International application No. PCT/US97/20539	International filing date (day/month/year) 07 November 1997 (07.11.97)	Priority date (day/month/year) 08 November 1996 (08.11.96)
Applicant PURDUE RESEARCH FOUNDATION et al		

The applicant is hereby notified of the date of receipt by the International Bureau of the priority document(s) relating to the following application(s):

Priority application No:	Priority date:	Priority country:	Date of receipt of priority document:
08/747,112	08 Nov 1996 (08.11.96)	US	03 Feb 1998 (03.02.98)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Céline Faust
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

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From the INTERNATIONAL BUREAU

To:

PAYNTER, L. Scott
Woodard, Emhardt, Naughton,
Moriarty & McNett
Bank One Center/Tower, Suite 3700
111 Monument Circle
Indianapolis, IN 46204
ETATS-UNIS D'AMERIQUE

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

Date of mailing (day/month/year)
14 May 1998 (14.05.98)

Applicant's or agent's file reference
PUR-63/75P

IMPORTANT NOTICE

International application No.	**International filing date** (day/month/year)	**Priority date** (day/month/year)
PCT/US97/20539	07 November 1997 (07.11.97)	08 November 1996 (08.11.96)

Applicant
PURDUE RESEARCH FOUNDATION et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
   AU,BR,CA,CN,EP,IL,JP,KP,KR,NO,PL,US

   In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
   AL,AM,AP,AT,AZ,BA,BB,BG,BY,CH,CU,CZ,DE,DK,EA,EE,ES,FI,GB,GE,GH,HU,ID,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NZ,OA,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZW
   The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 14 May 1998 (14.05.98) under No. WO 98/20323

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a **demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer
J. Zahra

Telephone No. (41-22) 338.83.38